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=> fil capl; d que 15
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inventors

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FILE COVERS 1907 - 1 Apr 2002  VOL 136 ISS 14
FILE LAST UPDATED: 30 Mar 2002  (20020330/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
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CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

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L1          148 SEA FILE=CAPLUS ABB=ON  LIPKOWSKI A?/AU
L2          678 SEA FILE=CAPLUS ABB=ON  CARR D?/AU
L3           17 SEA FILE=CAPLUS ABB=ON  L1 AND L2
L4        16419 SEA FILE=CAPLUS ABB=ON  P(A)(SUBSTANCE OR PEPTIDE#)
L5            7 SEA FILE=CAPLUS ABB=ON  L4 AND L3

=> fil medl biotechno confsci embase wpids
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=> d que 19
L1          148 SEA FILE=CAPLUS ABB=ON  LIPKOWSKI A?/AU
L2          678 SEA FILE=CAPLUS ABB=ON  CARR D?/AU
L6          183 SEA L1
L7         1528 SEA L2
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L8 39537 SEA P(A)(SUBSTANCE OR PEPTIDE#)
L9 11 SEA L6 AND L7 AND L8

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PROCESSING COMPLETED FOR L5
PROCESSING COMPLETED FOR L9
L12 8 DUP REM L5 L9 (10 DUPLICATES REMOVED)
ANSWERS '1-7' FROM FILE CAPLUS
ANSWER '8' FROM FILE MEDLINE

=> d ibib ab l12 1-8

L12 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2001:319743 CAPLUS
DOCUMENT NUMBER: 134:348628
TITLE: Novel chimeric analgesic peptides
INVENTOR(S): **Carr, Daniel B.; Lipkowski, Andrzej W.**; Kream, Richard; Misicka-Kesik, Aleksandra
PATENT ASSIGNEE(S): New England Medical Center Hospital, USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030371	A2	20010503	WO 2000-US29789	20001027
WO 2001030371	A3	20011122		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-428692 A 19991028
AB The present invention provides a novel chimeric peptide contg. an opioid peptide moiety and a nociceptive peptide moiety for producing analgesia.

L12 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
ACCESSION NUMBER: 2000:446235 CAPLUS
DOCUMENT NUMBER: 133:159812
TITLE: A **substance P**-opioid chimeric

peptide as a unique nontolerance-forming analgesic

AUTHOR(S): Foran, Stacy E.; **Carr, Daniel B.**; **Lipkowski, Andrzej W.**; Maszczynska, Iwona; Marchand, James E.; Misicka, Aleksandra; Beinborn, Martin; Kopin, Alan S.; Kream, Richard M.

CORPORATE SOURCE: Departments of Anesthesiology and Pharmacology and Experimental Therapeutics, New England Medical Center, Tufts University School of Medicine, Boston, MA, 02111, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(13), 7621-7626
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To elucidate mechanisms of acute and chronic pain, it is important to understand how spinal excitatory systems influence opioid analgesia. The tachykinin **substance P** (SP) represents the prototypic spinal excitatory peptide neurotransmitter/neuromodulator, acting in concert with endogenous opioid systems to regulate analgesic responses to nociceptive stimuli. We have synthesized and pharmacol. characterized a chimeric peptide contg. overlapping NH2- and COOH-terminal functional domains of the endogenous opioid endomorphin-2 (EM-2) and the tachykinin SP, resp. Repeated administration of the chimeric mol. YPFFGLM-NH2, designated ESP7, into the rat spinal cord produces opioid-dependent analgesia without loss of potency over 5 days. In contrast, repeated administration of ESP7 with concurrent SP receptor (SPR) blockade results in a progressive loss of analgesic potency, consistent with the development of tolerance. Furthermore, tolerant animals completely regain opioid sensitivity after post hoc administration of ESP7 alone, suggesting that coactivation of SPRs is essential to maintaining opioid responsiveness. Radioligand binding and signaling assays, using recombinant receptors, confirm that ESP7 can coactivate .mu.-opioid receptors (MOR) and SPRs in vitro. We hypothesize that coincidental activation of the MOR- and SPR-expressing systems in the spinal cord mimics an ongoing state of reciprocal excitation and inhibition, which is normally encountered in nociceptive processing. Due to the ability of ESP7 to interact with both MOR and SPRs, it represents a unique prototypic, anti-tolerance-forming analgesic with future therapeutic potential.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3

ACCESSION NUMBER: 2000:846128 CAPLUS

DOCUMENT NUMBER: 134:37424

TITLE: Inhibition of morphine tolerance development by a **substance P**-opioid peptide chimera

AUTHOR(S): Foran, Stacy E.; **Carr, Daniel B.**; **Lipkowski, Andrzej W.**; Maszczynska, Iwona; Marchand, James E.; Misicka, Aleksandra; Beinborn, Martin; Kopin, Alan S.; Kream, Richard M.

CORPORATE SOURCE: Departments of Anesthesiology and Pharmacology and Experimental Therapeutics, New England Medical Center, Tufts University School of Medicine, Boston, MA, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 295(3), 1142-1148
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The neuropeptide **substance P** (SP), apart from its

traditional role in spinal nociceptive processing, is an important regulatory effector of opioid-dependent analgesic processes. The present study stems from our original findings indicating that (1) pharmacol. administered SP mediates a strong inhibitory activity on the development of morphine tolerance in rats, and that (2) a novel SP-opioid peptide chimera YPFFGLM-NH2, designated ESP7, produces opioid-dependent analgesia without tolerance development. To further examine the effects of simultaneous activation of two distinct opposing spinal systems on opioid tolerance and the mechanisms underlying chimeric peptide function, a second SP-opioid chimera was synthesized. This chimera, designated ESP6 (YPFFPLM-NH2), contains overlapping domains of endomorphin-2 and SP, resp. ESP6 is distinguished from ESP7 by a glycine to proline substitution at position 5. Intrathecal administration of morphine sulfate (MS) with ESP6 leads to a prolongation of MS analgesia over a 5-day period. The analgesia produced by ESP6 and MS is opioid receptor-dependent, due to the ability of naltrexone to block the analgesic response. Furthermore, when ESP6 and MS are administered with concurrent NK-1 receptor blockade, a decay in analgesic potency similar to that seen with MS alone results. The presence of a proline in ESP6 appears to reduce its conformational flexibility, limit its potency at the .mu.-opioid receptor, and hinder its analgesic effectiveness alone. However, ESP6 represents a novel adjuvant for the maintenance of opioid analgesia over time and provides a means to predict the pharmacol. properties of a chimera from its structure.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
ACCESSION NUMBER: 1994:208521 CAPLUS
DOCUMENT NUMBER: 120:208521
TITLE: Spinal co-administration of peptide **substance P** antagonist increases antinociceptive effect of the opioid peptide biphalin
AUTHOR(S): Misterek, K.; Maszczynska, I.; Dorociak, A.; Gumulka, S. W.; **Carr, D. B.**; Szyfelbein, S. K.; **Lipkowski, A. W.**
CORPORATE SOURCE: Dep. Pharmacodyn., Med. Acad., Warsaw, 00927, Pol.
SOURCE: Life Sci. (1994), 54(14), 939-44
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Intrathecal injection of 0.25 .mu.g of undecapeptide **substance P** antagonist (SPA) produced transient antinociception with a peak effect at 5 min. Increasing the SPA dose resulted in neurotoxicity. Intrathecal injection of the opioid peptide biphalin (BIP) produced antinociception for over 3 h without neurotoxicity. Coadministration of SPA (at subtoxic doses) increased BIP's antinociceptive effect. Naltrexone reversed analgesia due to BIP alone as well as after BIP+SPA.

L12 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:720377 CAPLUS
DOCUMENT NUMBER: 130:61457
TITLE: Alternative forms of interaction of **substance P** and opioids in nociceptive transmission
AUTHOR(S): Maszczynska, Iwona; **Lipkowski, Andrzej W.**; **Carr, Daniel B.**; Kream, Richard M.
CORPORATE SOURCE: Neuropeptide Laboratory, Medical Research Centre, Polish Academy of Sciences, Warsaw, PL-00-784, Pol.
SOURCE: Lett. Pept. Sci. (1998), 5(5-6), 395-398
CODEN: LPSCEM; ISSN: 0929-5666
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Many years preclin. and clin. anat., pharmacol., and physiol. studies

suggest that **substance P** (SP)- and opioid-expressing neurons produce opposite biol. effects at the spinal level, i.e., nociception and antinociception, resp. However, in certain circumstances intrathecally administered SP is capable of reinforcing of spinal morphine analgesia and may therefore function as an opioid adjuvant in vivo. The SP dose-response curve of spinally administered SP follows a bell-shaped or inverted-U configuration, permitting pharmacol. dissocn. of opioid-potentiating and analgesic properties of SP from traditional hyperalgesic effects seen at significantly higher concns. This analgesic effect is blocked by naloxone but unaffected by transection of the spinal cord, thus demonstrating the lack of supraspinal modulation. The present report briefly describes both reinforcing and opposing interactions between multiple opioid systems and **substance P** at the spinal level. We propose that a likely mechanism underlying SP-mediated enhancement of opioid analgesia is the ability of SP to release endogenous opioid peptides within the local spinal cord environment.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:466124 CAPLUS
DOCUMENT NUMBER: 129:225804
TITLE: Dual functional interactions of **substance P** and opioids in nociceptive transmission: review and reconciliation
AUTHOR(S): Maszczynska, Iwona; **Lipkowski, Andrzej W.**; **Carr, Daniel B.**; Kream, Richard M.
CORPORATE SOURCE: Neuropeptide Laboratory, Medical Research Centre, Polish Academy of Sciences, Warsaw, 02-106, Pol.
SOURCE: Analgesia (Elmsford, N. Y.) (1998), 3(4), 259-268
CODEN: AALGEB; ISSN: 1071-569X
PUBLISHER: Cognizant Communication Corp.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 70 refs. For many years preclin. and clin. anat., pharmacol., and physiol. studies have suggested that **substance P** (SP)- and opioid-expressing neurons produce opposite biol. effects at the spinal level (i.e., nociception and antinociception, resp.). However, in certain circumstances and within designated concn. ranges intrathecally administered SP is capable of significant reinforcement of spinal morphine analgesia and may therefore function as an opioid adjuvant in vivo. The SP dose-response curve of spinally administered SP follows an inverted-U configuration, permitting pharmacol. dissocn. of opioid-potentiating and analgesic properties of SP from traditional hyperalgesic effects realized at significantly higher concns. This analgesic effect is blocked by naloxone but unaffected by transection of the spinal cord, thus demonstrating the lack of supraspinal modulation. The present review surveys both reinforcing and opposing interactions between multiple opioid systems and **substance P** at the spinal level, and proposes that a likely mechanism underlying SP-mediated enhancement of opioid analgesia is the ability of SP to release endogenous opioid peptides within the local spinal cord environment.

L12 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:351823 CAPLUS
DOCUMENT NUMBER: 122:123841
TITLE: Biological activities of a peptide containing both casomorphin-like and **substance P** antagonist structural characteristics
AUTHOR(S): **Lipkowski, A. W.**; **Carr, D. B.**; Misicka, A.; Misterek, K.
CORPORATE SOURCE: Harvard Medical School, Massachusetts General Hospital, Boston, MA, 02114, USA

Searched by Barb O'Bryen, STIC 308-4291

SOURCE: [Beta]-Casomorphins Relat. Pept. [Int. Symp.], 2nd (1994), 113-18
CODEN: 60UMAA
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A new strategy of searching for local (i.e., peripherally active) analgesics has been proposed pursuing the development of compds. which should possess low penetrability of biol. barriers and wide receptor selectivity. To follow this concept a new peptide has been synthesized contg. the C-terminal fragment of **substance P** antagonist and the N-terminal fragment of the casomorphin structure; Tyr-Pro-D-Phe-Phe-D-Phe-D-Trp-Met-NH2 (AWL 60). In vitro biol. activity, and in vivo effects, i.e. antinociception after intrathecal administration, suggest that the 2 hybridized portions of AWL 60 possess a strong synergistic effect.

L12 ANSWER 8 OF 8 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 91076290 MEDLINE
DOCUMENT NUMBER: 91076290 PubMed ID: 1701617
TITLE: Neuropeptides and pain.
AUTHOR: **Carr D B; Lipkowski A W**
CORPORATE SOURCE: Department of Anesthesia and Medicine (Endocrinology), Massachusetts General Hospital, Boston.
SOURCE: AGRESSOLOGIE, (1990 Apr) 31 (4) 173-7. Ref: 56
Journal code: 31I; 0121575. ISSN: 0002-1148.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199101
ENTRY DATE: Entered STN: 19910308
Last Updated on STN: 19960129
Entered Medline: 19910124
AB Peptides have recently been found to function as neuromodulators or neuromediators within nociceptive pathways at central and peripheral sites. More complex and varied in their chemistry compared to "classical" low molecular weight monoamine neurotransmitters, peptides may nonetheless co-exist with these within a single neuron. The biological activity of a peptide results from an "address" segment that permits receptor binding and a "message" segment that initiates reactions within the cell. Opioid peptides (endorphins) are derived from three precursors and act by altering ionic fluxes of potassium or calcium across cell membranes. Nonopioid peptides active in nociception include calcitonin and its gene-related peptide C.G.R.P., bradykinin, **substance P** , somatostatin, cholecystokinin, and corticotropin-releasing hormone, among others. Ongoing investigations show significant responses of several peptide systems in experimental models relevant to vascular pain. Although the creation of novel peptide analogues has therapeutic promise, their present clinical use must be cautious in light of reports of neurotoxicity after intraspinal application of some of these compounds in animal models.

=> fil reg; s 33507-63-0
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DICTIONARY FILE UPDATES: 31 MAR 2002 HIGHEST RN 403640-18-6

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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L13 1 33507-63-0
(33507-63-0/RN)

=> d sqide

L13 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN **33507-63-0** REGISTRY
CN Substance P (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 21: PN: WO0181408 SEQID: 44 claimed protein
CN L-Methioninamide, L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-L-phenylalanyl-L-phenylalanylglycyl-L-leucyl-
CN Neurokinin P
CN Substance P (1-11)
CN Substance P (peptide)
CN Substance P (smooth-muscle stimulant)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 11
NTE modified

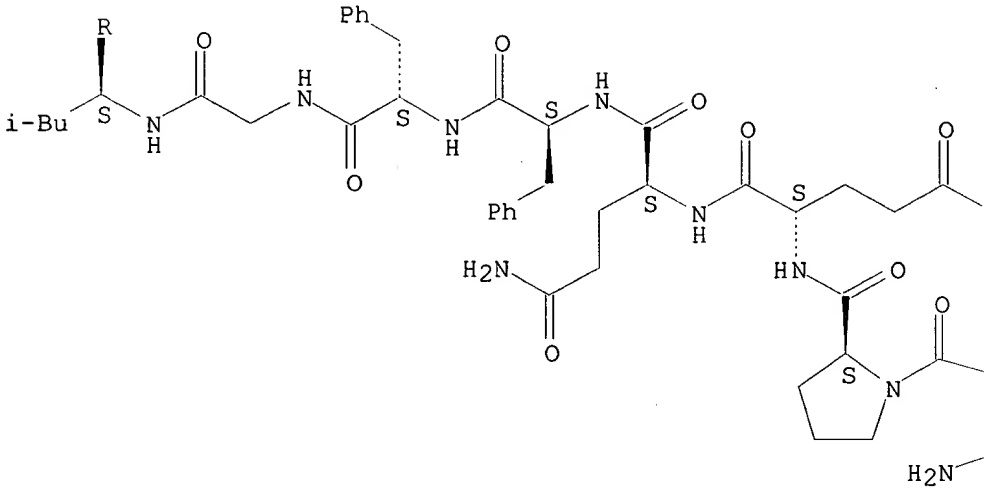
type	location	description
terminal mod.	Met-11 -	C-terminal amide

SEQ 1 RPKPQQFFGL M
DR 12769-48-1, 11035-08-8
MF C63 H98 N18 O13 S
CI COM
LC STN Files: ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, PROMT, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**

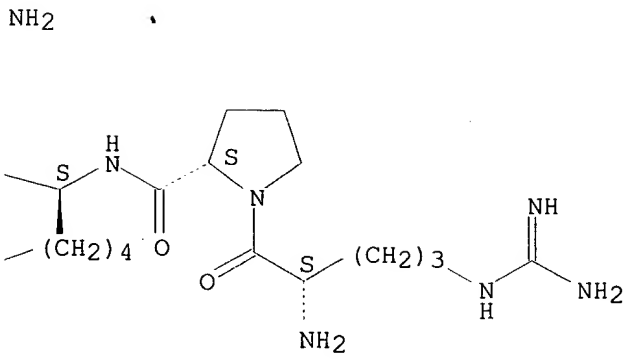
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.

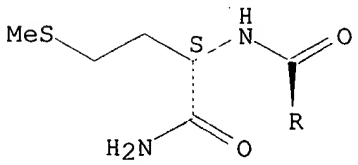
PAGE 1-A



PAGE 1-B



PAGE 2-A



12186 REFERENCES IN FILE CA (1967 TO DATE)
468 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

Searched by Barb O'Bryen, STIC 308-4291

12193 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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=> fil medl capl biotechno confsci embase wpids
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=> d que l17; d que l21; d que l22
L14        54287 SEA SUBSTANCE P
L15      1355761 SEA ?PEPTIDE?
L16       134651 SEA ANTIMICROBI? OR ANTI MICROBI?
L17           16 SEA L14 AND L15 AND L16



L14        54287 SEA SUBSTANCE P
L15      1355761 SEA ?PEPTIDE?
L20       200571 SEA ANTIBACTERI? OR ANTIFUNG? OR ANTI(W)(BACTERI? OR FUNGAL?)
L21           16 SEA L14 AND L15 AND L20



L14        54287 SEA SUBSTANCE P
L18         2299 SEA DEXTROROT? OR DEXTRO ROTAT?
L22            0 SEA L14 AND L18


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L23           31 L17 OR L21

=> dup rem l23
PROCESSING COMPLETED FOR L23
L25           24 DUP REM L23 (7 DUPLICATES REMOVED)
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                 ANSWERS '3-15' FROM FILE CAPLUS
                 ANSWERS '16-17' FROM FILE BIOTECHNO
                 ANSWER '18' FROM FILE EMBASE
                 ANSWERS '19-24' FROM FILE WPIDS

=> d ibib ab l25 1-24

L25  ANSWER 1 OF 24     MEDLINE                          DUPLICATE 2
ACCESSION NUMBER:    1999323992     MEDLINE
DOCUMENT NUMBER:     99323992   PubMed ID: 10395691
TITLE:               Neutrophil defensins induce histamine secretion from mast
                     cells: mechanisms of action.
AUTHOR:              Befus A D; Mowat C; Gilchrist M; Hu J; Solomon S; Bateman A
CORPORATE SOURCE:    Pulmonary Research Group, Department of Medicine,
                     University of Alberta, Edmonton, Canada..
```

dean.befus@ualberta.ca
SOURCE: JOURNAL OF IMMUNOLOGY, (1999 Jul 15) 163 (2) 947-53.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990806
Last Updated on STN: 20000303
Entered Medline: 19990729

AB Defensins are endogenous **antimicrobial peptides** stored in neutrophil granules. Here we report that a panel of defensins from human, rat, guinea pig, and rabbit neutrophils all have histamine-releasing activity, degranulating rat peritoneal mast cells with EC50 ranging from 70 to 2500 nM, and between 45 and 60% of the total histamine released. The EC50 for defensin-induced histamine secretion correlates with their net basic charge at neutral pH. There is no correlation between histamine release and **antimicrobial** potency. Degranulation induced by defensins has characteristics similar to those of activation by **substance P**. The maximum percent histamine release is achieved in <10 s, and it can be markedly inhibited by pertussis toxin (100 ng/ml) and by pretreatment of mast cells with neuraminidase. These properties differ from those for degranulation induced by IgE-dependent Ag stimulation and by the calcium ionophore A23187. GTPase activity, a measure of G protein activation, was induced in a membrane fraction from mast cells following treatment with defensin. Thus, neutrophil defensins are potent mast cell secretagogues that act in a manner similar to **substance P** and 48/80, through a rapid G protein-dependent response that is mechanistically distinct from Ag/IgE-dependent mast cell activation. Defensins may provide important pathways for communication between neutrophils and mast cells in defenses against microbial agents and in acute inflammatory responses.

L25 ANSWER 2 OF 24 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 96253865 MEDLINE
DOCUMENT NUMBER: 96253865 PubMed ID: 8963748
TITLE: The submandibular gland: a key organ in the neuro-immuno-regulatory network?.
AUTHOR: Sabbadini E; Berczi I
CORPORATE SOURCE: Department of Immunology, University of Manitoba, Winnipeg, Canada.
SOURCE: NEUROIMMUNOMODULATION, (1995 Jul-Aug) 2 (4) 184-202. Ref: 205
Journal code: CCL; 9422763. ISSN: 1021-7401.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961204

AB The evidence for the integration of the submandibular gland (SMG) into the neuroimmunoregulatory network has been reviewed. In laboratory rodents, factors extracted from the SMG were shown to stimulate lymphocyte proliferation, to affect the weight of the thymus, spleen and lymph nodes and to induce immunosuppression in several in vivo animal models. The SMG produces significant quantities of nerve growth factor (NGF), epidermal growth factor (EGF), transforming growth factor-beta and kallikreins, which are secreted into the saliva and affect immune and mucosal tissues

and nerve endings in the gastrointestinal tract. These factors play a role in regulating mucosal immuno/inflammatory response and in regeneration and healing. The major salivary glands also produce **antimicrobial** proteins and secretory IgA antibodies which are essential factors in mucosal host defense. SMG-derived NGF, EGF and glandular kallikrein are delivered into the bloodstream where they may act as important systemic immunoregulators and also have major regulatory influences on the central neuroendocrine system. There is evidence to indicate that EGF is involved in the regulation of gonadal function. Growth hormone, prolactin, androgens, thyroid hormone and corticosteroids regulate protein synthesis in the SMG, whereas secretory activity is regulated by sympathetic (alpha- and beta-adrenergic) parasympathetic (muscarinic) and **peptidergic** (**substance P** and vasoactive intestinal **peptide**) nerve fibers. Fluid and electrolyte secretion is promoted by parasympathetic, whereas protein secretion is stimulated by sympathetic nerve impulses. Steroid hormones and cytokines (interleukin-1 alpha, -beta, tumor necrosis factor, interferon-gamma) have a major regulatory influence on protein secretion, including the secretion of immunoglobulin into the saliva. The SMG interacts with the mucosal and systemic compartments of the immune system, with the central and peripheral nervous systems, with the pituitary gland, and with peripheral endocrine organs. These interactions enable the SMG to exert regulatory influences on immune/inflammatory reactions in the gastrointestinal tract, in the lungs, and possibly elsewhere. It is suggested that these functions make this gland a key regulatory organ in the neuroimmunoregulatory network. Evidence is increasing that the major salivary glands fulfill similar functions in other species, including humans.

L25 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
ACCESSION NUMBER: 1993:511952 CAPLUS
DOCUMENT NUMBER: 119:111952
TITLE: Characterization of the thermolysin-like cleavage of biologically active **peptides** by Xenopus laevis **peptide** hormone inactivating enzyme
AUTHOR(S): Joudiou, Carine; de Morais Carvalho, Krishnamurti; Camarao, Gisela; Boussetta, Hamadi; Cohen, Paul
CORPORATE SOURCE: Cent. Natl. Rech. Sci., Univ. Pierre et Marie Curie, Paris, 75006, Fr.
SOURCE: Biochemistry (1993), 32(23), 5959-66
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Peptide** hormone-inactivating endopeptidase (PHIE) is a metalloendopeptidase which was isolated from the skin granular gland secretions of Xenopus laevis. This peptidase exhibits a thermolysin-like character and hydrolyzes bonds on the N terminus of hydrophobic amino acids, performing cleavage of Xaa-Phe, Xaa-Leu, Xaa-Ile, Xaa-Tyr, and Xaa-Trp doublets. When the enzyme recognized a doublet of hydrophobic amino acids such as Phe6-Phe7 of somatostatin-14, Phe7-Phe8 of **substance P**, Phe4-Leu5 of [Leu5,Arg6]enkephalin, and Tyr4-Ile5 of angiotensin II, cleavage occurred preferentially between these residues. The use of selectively modified C-terminal **octapeptide** fragments of atrial natriuretic factor (ANF) indicated that the enzyme tolerates as substrates only **peptides** bearing a P'1 bulky hydrophobic amino acid residue. Although a P'1 hydrophobic residue was a necessary condition, it was found in a no. of **peptides** that all potential cleavage sites were not recognized by the enzyme. Apparently, this metalloendoprotease requires for its thermolysin-like activity a preferred conformation of the **peptide** chain. Kinetic results obtained using a series of related substrates derived from biol. active **peptides** of the atrial natriuretic factor, tachykinin, and enkephalin families indicated the presence of an extended binding site accommodating at least 6 amino acid residues, in

contrast to thermolysin (EC 3.4.24.4) and neutral endopeptidase (NEP; EC 3.4.24.11), which hydrolyze shorter homologous **peptides**. Since PHIE hydrolyzed the Lys12-Ile13 bond in PGLa, a major X. laevis skin secretion **antimicrobial** component (Km = 28 .mu.M), it is inferred that this novel enzyme, which is distinct from angiotensin-converting enzyme (ACE; EC 3.4.15.1), from meprin (EC 3.4.24.18), and from other presently known thermolysin-like metalloendoproteases, may play a role in the in vivo inactivation of biol. active **peptides**.

L25 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:107139 CAPLUS
DOCUMENT NUMBER: 136:163710
TITLE: Organ transplant media containing **antimicrobial polypeptides**
INVENTOR(S): Murphy, Christopher J.; Reid, Ted W.; McAnulty, Jonathan F.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009738	A1	20020207	WO 2001-US23785	20010727

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-221632P P 20000728
US 2000-249602P P 20001117
US 2001-290932P P 20010515

AB The present invention relates to media contg. purified **antimicrobial polypeptides**, such as defensins, and/or cell surface receptor binding proteins. The media may also contain buffers, macromol. oncotic agents, energy sources, impermeant anions, ATP substances. The media find use for the storage and preservation of internal organs prior to transplant.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:195116 CAPLUS
DOCUMENT NUMBER: 134:227146
TITLE: Use of a **substance P** antagonist in a cosmetic for prevention of skin sensitivity
INVENTOR(S): De la Charriere, Olivier; Breton, Lionel
PATENT ASSIGNEE(S): Societe L'Oreal S.A., Fr.
SOURCE: U.S., 9 pp., Cont. of U.S. Ser. No. 358,562, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6203803	B1	20010320	US 1997-881272	19970624
US 6235291	B1	20010522	US 1996-611549	19960311
US 6333042	B1	20011225	US 2000-584724	20000601
US 2001014342	A1	20010816	US 2000-735638	20001214

PRIORITY APPLN. INFO.: US 1994-358562 B1 19941214
FR 1995-5537 A 19950505
FR 1994-5537 A 19940505
US 1996-611549 A1 19960311
US 1997-881272 A1 19970624

AB The invention concerns the use of a **substance P** antagonist in a cosmetic compn. used to treat sensitive skin. More specifically, the invention relates to a **substance P** antagonist used to prevent and/or combat skin irritations, desquamation, erythemas, sensations of dysesthesia/overheating, or pruritus of the skin. A make-up removal face lotion contained Spantide II 5.00, antioxidant 0.05, isopropanol 40.00, preservative 0.30, and water q.s. 100%.

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:824291 CAPLUS
DOCUMENT NUMBER: 134:21425
TITLE: Protection of endogenous therapeutic **peptides** from peptidase activity through conjugation to blood components
INVENTOR(S): Bridon, Dominique P.; Ezrin, Alan M.; Milner, Peter G.; Holmes, Darren L.; Thibaudeau, Karen
PATENT ASSIGNEE(S): Conjuchem, Inc., Can.
SOURCE: PCT Int. Appl., 733 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000069900	A2	20001123	WO 2000-US13576	20000517
WO 2000069900	A3	20010215		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2000070665	A2	20001123	WO 2000-IB763	20000517
WO 2000070665	A3	20010419		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1105409	A2	20010613	EP 2000-936023	20000517

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

EP 1171582 A2 20020116 EP 2000-929748 20000517

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1999-134406P P 19990517
US 1999-153406P P 19990910
US 1999-159783P P 19991015
WO 2000-IB763 W 20000517
WO 2000-US13576 W 20000517

AB A method for protecting a **peptide** from peptidase activity in vivo, the **peptide** being composed of between 2 and 50 amino acids and having a C-terminus and an N-terminus and a C-terminus amino acid and an N-terminus amino acid is described. In the first step of the method, the **peptide** is modified by attaching a reactive group to the C-terminus amino acid, to the N-terminus amino acid, or to an amino acid located between the N-terminus and the C-terminus, such that the modified **peptide** is capable of forming a covalent bond in vivo with a reactive functionality on a blood component. The solid phase **peptide** synthesis of a no. of derivs. with 3-maleimidopropionic acid (3-MPA) is described. In the next step, a covalent bond is formed between the reactive group and a reactive functionality on a blood component to form a **peptide**-blood component conjugate, thereby protecting said **peptide** from peptidase activity. The final step of the method involves the analyzing of the stability of the **peptide**-blood component conjugate to assess the protection of the **peptide** from peptidase activity. Thus, the percentage of a K5 kringle **peptide** (Pro-Arg-Lys-Leu-Tyr-Asp-Lys-NH2) conjugated to human serum albumin via MPA remained relatively const. through a 24-h plasma assay in contrast to unmodified K5 which decreased to 9% of the original amt. of K5 in only 4 h in plasma.

L25 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:144719 CAPLUS
DOCUMENT NUMBER: 132:189686
TITLE: Inhibitors of dipeptidylpeptidase IV (DPP-IV) for regulation of substrate activity, and therapeutic use
INVENTOR(S): Wallner, Barbara
PATENT ASSIGNEE(S): Point Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000010549	A1	20000302	WO 1999-US18315	19990813
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9954801	A1	20000314	AU 1999-54801	19990813
BR 9913153	A	20010515	BR 1999-13153	19990813
EP 1104293	A1	20010606	EP 1999-941081	19990813
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

NO 2001000844 A 20010423 NO 2001-844 20010219
PRIORITY APPLN. INFO.: US 1998-97376P P 19980821
WO 1999-US18315 W 19990813

AB A method for regulating substrate (e.g. chemokine) activity in vivo is useful for the treatment of medical disorders such as inflammation, arteriolosclerosis and angiogenesis. The method involves the administration of an effective amt. of a DPP-IV inhibitor to a patient in need of such treatment.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:430595 CAPLUS
DOCUMENT NUMBER: 132:662
TITLE: Immunocytochemical localization of **substance P** neurokinin-1 receptors in rat gingival tissue
AUTHOR(S): Kido, Mizuho A.; Yamaza, Takayoshi; Goto, Tetsuya; Tanaka, T.
CORPORATE SOURCE: Faculty of Dentistry, First Department of Oral Anatomy, Kyushu University, Fukuoka, 812-8582, Japan
SOURCE: Cell & Tissue Research (1999), 297(2), 213-222
CODEN: CTSRCS; ISSN: 0302-766X
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The distributions of **substance P** (SP) and the neurokinin-1 receptor (NK1-R), the receptor preferentially activated by SP, were examd. in rat gingiva by immunocytochem. with light and electron microscopy. SP-immunoreactive nerve fibers were located preferentially in the junctional epithelium (JE) but few in the other oral and oral sulcular epithelia. NK1-R immunoreactivity was found in the endothelial cells (capillaries and postcapillary venules underlying the JE). NK1-R-labeled and -unlabeled unmyelinated nerve fibers were located close to the blood vessels and partially or completely covered by a Schwann cell sheath. In the JE, labeled naked axons without Schwann cell sheaths were obsd. Neutrophils and macrophages in the connective tissue underlying the JE and in the JE were also labeled with NK1-R. Furthermore, NK1-R was found in the JE cells. Basically, immunoreaction products for NK1-R were found throughout various cells (endothelial cells, neutrophils, and JE cells) at invaginations of the plasma membrane and in vesicular and granular structures that are probably endosomes and are found close to both the plasma membrane and the nucleus. This is a first report, demonstrating the presence of NK1-R in the gingival tissue in the normal nonstimulated condition. Furthermore, it is thought that SP may modulate the permeability of blood vessels beneath the JE, the prodn. of **antimicrobial** agents in neutrophils, and the proliferation and endocytic ability of JE cells through NK1-R.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:285049 CAPLUS
DOCUMENT NUMBER: 131:126165
TITLE: Identification and characterization of endopeptidase in Porphyromonas gingivalis
AUTHOR(S): Mochizuki, Hajime
CORPORATE SOURCE: Department of Preventive Dentistry, Kyushu Dental College, Kitakyushu, Japan
SOURCE: Kyushu Shika Gakkai Zasshi (1999), 53(1), 203-214
CODEN: KSGZA3; ISSN: 0368-6833
PUBLISHER: Kyushu Shika Gakkai
DOCUMENT TYPE: Journal

Searched by Barb O'Bryen, STIC 308-4291

LANGUAGE: Japanese

AB Porphyromonas gingivalis is one of major etiol. agents of progressive periodontal disease and has several proteolytic enzymes implicated in invasion, tissue destruction and evasion of host **antibacterial** defenses. The aim in our lab. is to fully clarify the role of enzymes in relation to pathogenesis of this bacterium. In the previous study, we detd. the nucleotide sequence of clone pAL2 obtained from P. gingivalis 381 (Microbiol. 141: 2047-2052, 1995), which appeared to contain a DNA fragment encoding a proteolytic enzyme. An approx. 3.8 kb DNA fragment (pAL2) was sequenced, the DNA sequence anal. revealed one complete ORF (pepO) and two incomplete ORFs in this fragment. ORF (pepO) encoded a protein (P. gingivalis PepO) of 690 amino acids with a calcd. mol. wt. of 78,796. A comparison of the amino acid sequence of P. gingivalis PepO with other proteins in the SWISS-PROT database revealed a 31.7% identity with Endothelin-Converting Enzyme 1 (ECE 1), one of the NEP families. Polymerase chain reaction (PCR) was performed for amplification of pepO, and the PCR fragment was cloned into pET-3a in order to overexpress P. gingivalis PepO in E. coli BL21 (DE3). The overexpressed P. gingivalis PepO was purified to apparent homogeneity by ion-exchange chromatog. and gel filtration. The optimal pH of the purified enzyme was between 6.8 and 7.2, and the optimal temp. range was between 40 .degree.C and 50 .degree.C. The activity was strongly inhibited by the NEP inhibitor phosphoramidon, but only slightly by the NEP inhibitor thiorphan, like ECE 1. The purified enzyme hydrolyzed met-enkephalin, bradykinin and **substance P**, which were physiol. **peptides**, like NEP from Lactococcus lactis. And the enzyme cleaved big endothelin (ET)-1, big ET-2 and big ET-3, so that generated ET1, ET2 and ET3. The ECE1 is a key enzyme during processing for generating ET1 which acts as a mitogen as well as a vasoconstrictor for vascular smooth muscle cells. Therefore, these results suggest that P. gingivalis PepO might operate as a virulence factor of not only periodontitis but cardiovascular diseases.

L25 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:87631 CAPLUS
DOCUMENT NUMBER: 128:149985
TITLE: **Substance P** treatment for immunostimulation
INVENTOR(S): Witten, Mark L.; Harris, David T.
PATENT ASSIGNEE(S): Witten, Mark L., USA; Harris, David T.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9803194	A2	19980129	WO 1997-US13146	19970708
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5945508	A	19990831	US 1997-829445	19970328
AU 9740464	A1	19980210	AU 1997-40464	19970708
AU 737201	B2	20010809		
EP 957930	A2	19991124	EP 1997-938049	19970708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

US 5998376 A 19991207 US 1998-28003 19980223
PRIORITY APPLN. INFO.: US 1996-22063P P 19960723
US 1997-829445 A 19970328
WO 1997-US13146 W 19970708

AB **Substance P** aerosols are effective in replenishing immune systems compromised by environmental toxicants. They are also useful for prophylaxis against and treatment of infections and neoplasms. They are useful for accelerating maturation of immune systems or maintaining immune function, as well. Chronic exposure to hydrocarbons is particularly damaging to the immune system, and thus this occupational hazard can be counteracted by treatment with **substance P** aerosols.

L25 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:394693 CAPLUS
DOCUMENT NUMBER: 129:157188
TITLE: Effect of **substance P** on the functions of human polymorphonuclear neutrophilic leukocytes
AUTHOR(S): Zhou, Wuqing; Fa, Xiangguang; Jiang, Xin; Lu, Shihong
CORPORATE SOURCE: Inst. Dermatol. Chinese Union Med. College, Nanjing, 210042, Peop. Rep. China
SOURCE: Zhonghua Weishengwuxue He Mianyixue Zazhi (1998), 18(2), 124-127
CODEN: ZWMZDP; ISSN: 0254-5101
PUBLISHER: Weishenbu Beijing Shengwu Zhipin Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The **neuropeptide substance P** (SP) might affect some of the functions of polymorphonuclear neutrophilic leukocytes (PMN) involving inflammation and immunity regulation. In this study, we detd. that SP increased the prodn. of O2-, H2O2 and NO, and the activity of a functional enzyme neutral endopeptidase (NEP) and the membrane fluidity of human PMN with or without the presence of bacterial chemoattractant FMLP-Me. The results showed that SP(.gtoreq.10-5 mol/L) alone could stimulate PMN to produce O2-, H2O2 and NO, which was inhibited by N-monomethyl-L-arginine; SP (10-6.apprx.10-4 mol/L) promoted H2O2 prodn. of PMN in response to FMLP-Me in a dose-dependent manner, but downregulated the NEP activity synergized with FMLP-methyl; SP promoted the membrane fluidity of PMN. These data indicated that SP could modulate inflammation by PMN and potentiate the **antimicrobial** function of PMN. Furthermore, SP affecting PMN functions might be a pathway by which nerve system regulated inflammatory and immune reactions.

L25 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:296920 CAPLUS
DOCUMENT NUMBER: 126:277779
TITLE: Libraries of backbone-cyclized peptidomimetics
INVENTOR(S): Hornik, Vered; Gilon, Chaim
PATENT ASSIGNEE(S): Peptor Limited, Israel; Yissum Research Development Company of the Hebrew University; Hornik, Vered; Gilon, Chaim
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9709344	A2	19970313	WO 1996-IL91	19960828
WO 9709344	A3	19970522		

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA

US 6117974	A	20000912	US 1995-569042	19951207
AU 9668361	A1	19970327	AU 1996-68361	19960828
AU 714917	B2	20000113		
JP 11500741	T2	19990119	JP 1996-511044	19960828
EP 923601	A2	19990623	EP 1996-928663	19960828

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.:	IL 1995-115096	A	19950829
	US 1995-569042	A	19951207
	IL 1991-99628	A	19911002
	US 1992-955380	B2	19921001
	US 1995-444135	A2	19950518
	WO 1996-IL91	W	19960828

OTHER SOURCE(S): MARPAT 126:277779

AB Libraries of novel backbone-cyclized **peptide** analogs are formed by means of bridging groups attached via the alpha nitrogens of amino acid derivs. to provide novel non-peptidic linkages. Novel building units used in the synthesis of these backbone-cyclized **peptide** analogs are N.alpha. (.omega.-functionalized) amino acids constructed to include a spacer and a terminal functional group. One or more of these N.alpha. (.omega.-functionalized) amino acids are incorporated into a library of **peptide** sequences, preferably during solid phase **peptide** synthesis. The reactive terminal functional groups are protected by specific protecting groups that can be selectively removed to effect either backbone-to-backbone or backbone-to-side chain cyclizations. The invention is exemplified by libraries of backbone-cyclized bradykinin analogs, somatostatin analogs, BPI analogs and **Substance P** analogs having biol. activity. Further embodiments of the invention are Interleukin-6 receptor derived **peptides** having ring structures involving backbone cyclization.

L25 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1997:429525 CAPLUS
DOCUMENT NUMBER:	127:55889
TITLE:	Pharmaceutical and cosmetic compositions containing .alpha.-TNF antagonists for treatment of skin redness of neurogenic origin
INVENTOR(S):	De Lacharriere, Olivier; Breton, Lionel
PATENT ASSIGNEE(S):	L'Oreal S. A., Fr.
SOURCE:	Eur. Pat. Appl., 10 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	French
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 774250	A1	19970521	EP 1996-402291	19961028
EP 774250	B1	19981125		

R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE

FR 2741262	A1	19970523	FR 1995-13729	19951120
FR 2741262	B1	19990305		
CA 2235038	AA	19970529	CA 1996-2235038	19961028
WO 9718799	A1	19970529	WO 1996-FR1688	19961028

W: BR, CA, CN, HU, JP, KR, MX, PL, RU

AT 173620	E	19981215	AT 1996-402291	19961028
CN 1202822	A	19981223	CN 1996-198450	19961028
JP 11501665	T2	19990209	JP 1996-519429	19961028
ES 2127613	T3	19990416	ES 1996-402291	19961028
US 5895649	A	19990420	US 1996-752551	19961120

PRIORITY APPLN. INFO.: FR 1995-13729 A 19951120
WO 1996-FR1688 W 19961028

AB Pharmaceutical and cosmetic compns. contg. .alpha.-tumor necrosis factor (.alpha.-TNF) antagonists for treatment of skin redness of neurogenic origin such as rosacea. A cream contained lisophyllin 0.5, glycerol stearate 2, Polysorbate-60 1, stearic acid 1.4, triethanolamine 0.7, carbomer 0.4, cyclomethicone 8, sunflower oil 12, antioxidants 0.05, preservatives 0.3, and water q.s. 100%.

L25 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:195630 CAPLUS
DOCUMENT NUMBER: 126:190940
TITLE: Topical pharmaceutical compositions containing volatile oils, silicones, and active ingredients
INVENTOR(S): Grollier, Jean-Francois; Allec, Josiane; Agostini, Isabelle
PATENT ASSIGNEE(S): L'Oreal S. A., Fr.
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 755675	A1	19970129	EP 1996-401491	19960705
EP 755675	B1	19970917		
R: DE, ES, FR, GB, IT				
FR 2737118	A1	19970131	FR 1995-9252	19950728
FR 2737118	B1	19970905		
ES 2109832	T3	19980116	ES 1996-401491	19960705
AU 9659430	A1	19970213	AU 1996-59430	19960710
AU 679663	B2	19970703		
CA 2182226	AA	19970129	CA 1996-2182226	19960726
JP 09040548	A2	19970210	JP 1996-198146	19960726
JP 2965510	B2	19991018		
US 6136332	A	20001024	US 1996-688027	19960729

PRIORITY APPLN. INFO.: FR 1995-9252 A 19950728
OTHER SOURCE(S): MARPAT 126:190940
AB The title pharmaceutical contg. volatile oils, Ph silicones, and active ingredients are claimed. A pliable paste contained cyclopentadimethylsiloxane 45, polyphenylmethylsiloxane 25, silicone wax 10, polyethylene wax 5, alkyl dimethicone 5, titanium dioxide 5, Nylon 3, and fusidic acid 2g.

L25 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:204743 CAPLUS
DOCUMENT NUMBER: 112:204743
TITLE: Formulations for the rectal and vaginal administration of biologically active **peptides**
INVENTOR(S): Kossowicz, Joachim; Hacker, Elke; Milde, Karl; Loesse, Guenter; Mueller, Frank
PATENT ASSIGNEE(S): VEB Berlin-Chemie, Ger. Dem. Rep.
SOURCE: Ger. (East), 4 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German

Searched by Barb O'Bryen, STIC 308-4291

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 273980	A1	19891206	DD 1988-317829	19880712
DD 273980	B5	19940414		
DK 8903414	A	19900113	DK 1989-3414	19890711
JP 03047114	A2	19910228	JP 1989-177282	19890711
EP 371195	A1	19900606	EP 1989-112726	19890712
EP 371195	B1	19930929		
R: DE, ES, FR, GB, IT, SE				
CA 1332349	A1	19941011	CA 1989-605464	19890712
ES 2059649	T3	19941116	ES 1989-112726	19890712

PRIORITY APPLN. INFO.: DD 1988-317829 19880712

AB Controlled-release forms of biol. active **peptides** (e.g., insulin or **substance P**) for rectal or vaginal administration comprise the **peptide** bound to a high-mol.-wt. carrier, as well as the presence of an absorption promoter, a protease inhibitor, and an **antibacterial** agent. Thus, suppositories were prepd. which contained agar-bound insulin, lauroylleucine (absorption enhancer), metronidazole (**antibacterial**) and aprotinin (protease inhibitor).

L25 ANSWER 16 OF 24 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 2001:32322685 BIOTECHNO
TITLE: APAP, a sequence-pattern recognition approach identifies **substance P** as a potential apoptotic **peptide**
AUTHOR: Del Rio G.; Castro-Obregon S.; Rao R.; Ellerby H.M.; Bredesen D.E.
CORPORATE SOURCE: D.E. Bredesen, Buck Institute for Age Research, 8001 Redwood Blvd., Novato, CA 94945-1400, United States. E-mail: dbredesen@buckinstitute.org
SOURCE: FEBS Letters, (13 APR 2001), 494/3 (213-219), 26 reference(s)
CODEN: FEBLAL ISSN: 0014-5793
PUBLISHER ITEM IDENT.: S0014579301023481
DOCUMENT TYPE: Journal; Article
COUNTRY: Netherlands
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We have previously described a novel cancer chemotherapeutic approach based on the induction of apoptosis in targeted cells by homing pro-apoptotic **peptides**. In order to improve this approach we developed a computational method (approach for detecting potential apoptotic **peptides**, APAP) to detect short PAPs, based on the prediction of the helical content of **peptides**, the hydrophobic moment, and the isoelectric point. PAPs are toxic against bacteria and mitochondria, but not against mammalian cells when applied extracellularly. Among other **peptides**, **substance P** was identified as a PAP and subsequently demonstrated to be a pro-apoptotic **peptide** experimentally. APAP thus provides a method to detect and ultimately improve pro-apoptotic **peptides** for chemotherapy. .COPYRGT. 2001 Published by Elsevier Science B.V.

L25 ANSWER 17 OF 24 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 1992:22240271 BIOTECHNO
TITLE: WS9326A, a novel tachykinin antagonist isolated from Streptomyces violaceusniger No. 9326 I. Taxonomy, fermentation, isolation, physico-chemical properties and biological activities
AUTHOR: Hayashi K.; Hashimoto M.; Shigematsu N.; Nishikawa M.;

Ezaki M.; Yamashita M.; Kiyoto S.; Okuhara M.; Kohsaka M.; Imanaka H.
CORPORATE SOURCE: Exploratory Research Laboratories, Fujisawa Pharmaceutical Co Ltd, 5-2-3 Tokodai,Tsukuba City, Ibaraki 300-26, Japan.
SOURCE: Journal of Antibiotics, (1992), 45/7 (1055-1063)
CODEN: JANTAJ ISSN: 0021-8820
DOCUMENT TYPE: Journal; Article
COUNTRY: Japan
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Data from several studies suggest that tachykinins may play an important role in the pathophysiology of airway diseases, especially asthma. Our aim is to discover tachykinin antagonists which exhibit therapeutically useful anti-asthmatic activity. In our search for activities inhibiting the binding of .cents..sup.3H!**substance P** to guinea-pig lung membrane preparations, we have found that the fermentation product, WS9326A, isolated from Streptomyces violaceusniger, is a potent tachykinin receptor antagonist.

L25 ANSWER 18 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92295258 EMBASE
DOCUMENT NUMBER: 1992295258
TITLE: Human nasal host defense and sinusitis.
AUTHOR: Kaliner M.A.; Druce H.M.; Irvin C.G.; Rachelefsky G.S.
CORPORATE SOURCE: Allergic Diseases Section, NIAID, National Institutes of Health,Bethesda, MD 20892, United States
SOURCE: Journal of Allergy and Clinical Immunology, (1992) 90/3 II (424-430).
ISSN: 0091-6749 CODEN: JACIBY
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 011 Otorhinolaryngology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Sinusitis is an exceptionally common disorder that affects an estimated 35 million Americans per year. The development of sinusitis requires both the presence of a virulent pathogen and the failure of the local immune system to prevent or effectively combat the infection. Identification of the components of the immune defense system of the upper respiratory tract and the possible areas of dysfunction that predispose to sinusitis may be important steps in the eventual prevention of this common disease. The nasal and sinus passages are lined by respiratory mucous membranes. Recent studies have identified some of the constituents found in mucus and their roles in human health and disease. However, the local immune system of the respiratory mucosa is largely unknown, and its role in sinusitis is conjectural. Nasal secretions include many proteins that serve important functions in local mucosal host defense. Most of these host-defense molecules are synthesized and secreted by serous cells in the submucous glands, and it appears that the serous cell is the resident **antimicrobial** cell in mucous membranes. Currently data suggest that serous cell secretion is abnormal in patients with recurrent sinusitis and that effective treatment leads to correction of the secretory abnormality along with improvement in sinusitis.

L25 ANSWER 19 OF 24 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-624275 [72] WPIDS
CROSS REFERENCE: 2001-450491 [48]
DOC. NO. CPI: C2001-186121
TITLE: Composition useful for reducing or preventing the impairment of intestinal or respiratory tract mucosal

immunity comprises a **neuropeptide**.

DERWENT CLASS: B04
INVENTOR(S): KUDSK, K A
PATENT ASSIGNEE(S): (UYTE-N) UNIV TENNESSEE RES CORP
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6271202	B1	20010807	(200172)*		9

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6271202	B1	Provisional	US 1996-15835P	19960419
		Provisional	US 1996-29689P	19961031
		CIP of	US 1997-842877	19970417
			US 1998-67032	19980428

PRIORITY APPLN. INFO: US 1998-67032 19980428; US 1996-15835P 19960419; US 1996-29689P 19961031; US 1997-842877 19970417

AB US 6271202 B UPAB: 20011206

NOVELTY - A composition comprises a **neuropeptide**.

DETAILED DESCRIPTION - A composition comprises a **neuropeptide** consisting Trp-Ala-Val-Gly-His-Leu-Met-NH2 (I) and a carrier.

An INDEPENDENT CLAIM is also included for reducing the rate of infection of the respiratory tract by a pathogenic microorganism (preferably virus, bacterium or fungus) in an animal associated with a lack of enteral feeding or a lack or immunological stimulation of the gastrointestinal tract (GI) involving administering a **neuropeptide**, a compound which stimulates the release of **neuropeptide** or a compound which is released in response to a **neuropeptide** selected from bombesin, gastrin-releasing **polypeptide** and/or a **neuropeptide** having an amino acid C terminus corresponding to (I).

ACTIVITY - Viricide; **Antifungal; Antibacterial;** Respiratory.

MECHANISM OF ACTION - Respiratory tract pathogens inhibitor.

55 mice underwent intranasal inoculation with liposomes (LIP) alone (no immunization) or LIP-containing Pseudomonas aeruginosa (pneumonia (Ps.) antigen (PS)). After 10 days, PS mice were catheterized and randomized to chow (n = 15), IV-total parenteral nutrition (TPN) (n = 14), or IV-TPN with 15 micro g/k tid bombesin (BBS) (n = 14). Diets began on the third postoperative day. LIP mice received chow but no catheter. After 5 days of diet, all mice were given a 100% lethal dose (LD100) of live intratracheal Ps (1.2 multiply 108 bacteria). The mortality (number of expired animals/total number of animals) at 48 of PS mice received was chow, IV-TPN and BBS-IV-TPN were 3/15, 12/14 and 3/14 respectively and of LIP mice received chow was 11/12. Thus Ps. immunization reduced mortality from 92% (LIP) to 20% (chow), but IV-TPN increased mortality (86%) to that of unimminized animals. BBS prevents this increased mortality. BBS maintains respiratory immunity in Ps. immune IV-TPN mice.

USE - For reducing the rate of infection of the respiratory tract by the pathogenic microorganism (claimed), for reducing the impairment of respiratory tract mucosal immunity and reducing the atrophy or dysfunction of the small intestinal GALT and generalized mucosal immunity of an animal associated with a lack of enteral feeding or a lack of immunological stimulation of GI tract.

ADVANTAGE - The **neuropeptide** attenuate TPN-associated depression of B- and T- cell populations within the small intestine, increases intestinal IgA, and prevents depression of the CD4+/CD8+ ratio

of the cells within the lamina propria. Also attenuate TPN-induced GALT atrophy.
Dwg.0/4

L25 ANSWER 20 OF 24 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-450491 [48] WPIDS
CROSS REFERENCE: 2001-624275 [53]
DOC. NO. CPI: C2001-136033
TITLE: Reducing impairment of respiratory tract mucosal immunity related to lack of enteral feeding or immunological stimulation of gastrointestinal tract, in an animal, by administering a **neuropeptide** e.g. bombesin.
DERWENT CLASS: B04 D16
INVENTOR(S): KUDSK, K A
PATENT ASSIGNEE(S): (UYTE-N) UNIV TENNESSEE RES CORP
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6262027	B1	20010717	(200148)*		15

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6262027	B1	Provisional	US 1996-15835P	19960419
		Provisional	US 1996-29689P	19961031
		CIP of	US 1997-842877	19970417
		Div ex	US 1998-67032	19980428
			US 1999-473355	19991228

PRIORITY APPLN. INFO: US 1999-473355 19991228; US 1996-15835P 19960419; US 1996-29689P 19961031; US 1997-842877 19970417; US 1998-67032 19980428

AB US 6262027 B UPAB: 20011211
NOVELTY - Reducing impairment of respiratory tract mucosal immunity in an animal associated with lack of enteral feeding or immunological stimulation of gastrointestinal tract, by administering a **neuropeptide** (NP), e.g. bombesin, gastrin releasing **polypeptide** and/or NP having a specific amino acid C terminus or a compound which stimulates release of NP or a compound released in response to NP.

DETAILED DESCRIPTION - Reducing impairment of respiratory tract mucosal immunity in an animal associated with lack of enteral feeding or immunological stimulation of gastrointestinal tract, comprises administering a **neuropeptide** (NP), such as bombesin, gastrin releasing **polypeptide**, NP having a specific amino acid C terminus and their mixtures or a compound which stimulates release of NP or a compound released in response to NP. The NP having the amino acid C terminus corresponding to the sequence WAVGHLM is administered to the animal.

An INDEPENDENT CLAIM is also included for a composition useful in reducing impairment of respiratory tract mucosal immunity comprising a therapeutically effective amount of NP, a compound that stimulates the release of NP or which is released in response to NP.

ACTIVITY - Antiinflammatory; **Antibacterial**; Virucide; Fungicide.

MECHANISM OF ACTION - Regulator of cellular immunity and stimulator of nasal mucus and serous cell secretions.

To demonstrate that bombesin (BBS) prevents the total parenteral nutrition (TPN)-induced gut-associated lymphoid tissue (GALT) atrophy,

depressed gastrointestinal (GI) and respiratory tract (RT) immunoglobulin (Ig)-A levels and impaired nasal antiviral IgA-mediated mucosal immunity, mice models were used. Mice were administered A/PR8-Mt.Sinai (H1N1) virus, a mouse-adapted influenza strain. Following a three week period of convalescence, the mice underwent placement of catheters for intravenous (IV) infusion after intraperitoneal injection of Ketamine and acepromazine maleate mixture.

A silicone rubber catheter was inserted into the vena cava through the right jugular vein. Catheterized mice were connected to an infusion apparatus and saline infused. The chow group served as the control group and received an infusion of physiologic saline in addition to standard laboratory mouse diet.

TPN group received a standard TPN solution intravenously. After 5 days of IV TPN, the mice received 1,2 or 3 days of 15 micro g/kg BBS intravenously. The mice were then sacrificed to harvest lymphocytes from Peyer's patches (PP), intraepithelial (IE) and lamina propia (LP) for cell yields.

The GI and RT IgA levels were analyzed by enzyme linked immunosorbant assay (ELISA). The results showed a PP multiply 106 cell count of 4.4 plus or minus 1.9 in TPN group and 7.6 plus or minus 2.3 in TPN-BBS group, IE multiply 105 cell count of 3.6 plus or minus 1.1 in TPN group and 6.1 plus or minus 0.9 in TPN-BBS group and LP multiply 106 cell count of 4.1 plus or minus 1.9 in TPN group and 6.2 plus or minus 1.4 in TPN-BBS group. The GI IgA (micro g) levels for TPN and TPN-BBS was 42 plus or minus 23 and 111 plus or minus 55 and respiratory tract IgA (ng) for TPN and TPN-BBS was 284 plus or minus 42 and 528 plus or minus 88, respectively.

USE - The method is useful for reducing, preferably eliminating, impairment of respiratory tract mucosal immunity and in particular upper and lower respiratory mucosal immunity, associated with a lack of enteral feeding of complex diets (e.g. Chow or complex enteral diet) or lack of immunological stimulation of gastrointestinal (GI) tract in animals and preventing infection of respiratory tract caused by pathogenic viruses, bacteria, fungi, etc. Risk of infections such as pneumonia occurring in the upper and lower respiratory tract may be reduced or prevented by this method.

Also it is useful for reducing the atrophy or dysfunction of the small intestinal gut-associated lymphoid tissue (GALT) of an animal associated with lack of enteral feeding or immunological stimulation of GI tract.

Dwg.0/0

L25 ANSWER 21 OF 24 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-015586 [02] WPIDS
DOC. NO. CPI: C2001-004083
TITLE: Treating inflammation, particularly antigen driven, immune-mediated inflammation and neurogenic inflammation, comprises administering manzamine compounds e.g. manzamine A.
DERWENT CLASS: B02
INVENTOR(S): GUNASEKERA, S P; MAYER, A M S; POMPONI, S A; SENNETT, S H
PATENT ASSIGNEE(S): (HARB-N) HARBOR BRANCH OCEANOGRAPHIC; (UYMI-N) UNIV MIDWESTERN
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000056304	A2	20000928	(200102)*	EN	31
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: CA JP					
EP 1162970	A2	20011219	(200206)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000056304	A2	WO 2000-US7974	20000324
EP 1162970	A2	EP 2000-919646	20000324
		WO 2000-US7974	20000324

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 1162970	A2	Based on	WO 200056304

PRIORITY APPLN. INFO: US 1999-164294P 19991108; US 1999-125903P 19990324

AB WO 200056304 A UPAB: 20010110

NOVELTY - Treating inflammation in a human or animal comprises administering manzamine compounds (I)-(V), their salts, analogs or derivatives.

DETAILED DESCRIPTION - Treating inflammation in a human or animal comprises administering manzamine compounds of formula (I)-(V), their salts, analogs or derivatives.

X1-X6 = H, halo, OH, lower alkoxy, lower acyloxy or lower mono- or dialkylamino;

R1 = H, lower alkyl or lower acyl;

R2 = H, OH, lower alkoxy or lower acyloxy;

X1'-X6' = H, halo, OH, lower alkoxy, lower acyloxy, thiol, lower alkylthiol, nitro, amino, lower alkylsulfonyl, aminosulfonyl, SO3H, lower acylamino, lower alkyl, or lower monoalkyl or dialkylamino;

R1', R2' = as for R1;

Y = H, OH, lower alkoxy or acyloxy;

R = H, halo, OH or lower acyloxy;

X = oxo or any 2 of H, OH, lower alkyl, lower alkoxy, lower acyloxy, where lower = 1-5C.

INDEPENDENT CLAIMS are also included for the following:

(1) treating a condition in a human or an animal comprising administering (I)-(V) where the condition is pain, burns, allergic responses, wound healing, anaphylactic reactions, inflammatory bowel disease, nephritis, conjunctivitis, inflammatory gum disease, neurogenic inflammation, meningitis, septic shock, Down's syndrome, post ischemic brain injury, HIV encephalopathy, Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerosis, multiple sclerosis, acute asthmatic attack and inflammation of the lung due to chemical exposure;

(2) a composition comprising a compound selected from (I)-(V) (sic).

ACTIVITY - Antiinflammatory; analgesic; vulnerary; nephrotropic; antiinflammatory; **antibacterial**; immunosuppressive; antiparkinsonian; anti-HIV; nootropic; neuroprotective; antiviral; antiasthmatic.

MECHANISM OF ACTION - Inhibitors of antigen driven, immune-mediated inflammation and neurogenic inflammation activity (neurogenic inflammation can be evoked by **neuropeptides** such as **substance P**, calcitonin gene-related **peptide**, vasoactive intestinal **peptide** and neurokinin A); inhibitors of microglia (Bm phi) O2- generation; inhibitors of Bm phi thromboxane B2 (TXB2) generation.

Manzamine A-F inhibited Bm phi O2- generation with IC50 values of 0.1, plus or minus 5, plus or minus 5, plus or minus 5, more than 10 and more than 10 micro M, respectively. Manzamine A-F also inhibited Bm phi TXB2 generation with IC50 values of less than 0.1, plus or minus 3, plus or minus 5, plus or minus 0.3, 10, and much greater than 10 respectively, and caused release of LDH in a toxicity assay which assessed Bm phi viability with IC50 values of greater than 30, plus or minus 3, plus or

minus 5, plus or minus 0.5, more than 10, and more than 10, respectively. (In all these assays, manzamine A (Ia) exhibited more potent inhibitory activity on O2- and TXB2 than B-F and was less toxic than manzamine B-F).

USE - For treating inflammation in which the primary activating inflammation is antigen-derived or of neurogenic origin. For pain, burns, allergic responses, wound healing, anaphylactic reactions, inflammatory bowel disease, nephritis, conjunctivitis, inflammatory gum disease, neurogenic inflammation, meningitis, septic shock, Down's syndrome, post ischemic brain injury, HIV encephalopathy, Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerosis, multiple sclerosis, acute asthmatic attack and inflammation of the lung due to chemical exposure. In (1), the pain is migraine, rhinitis, thermal induced pain, radiation induced pain or chemical induced pain; the burn is chemical burns, chemical induced lesions, radiation burns and thermal burns; and the treatment facilitates the promotion of wound healing (all claimed). The manzamine compounds may also be used as intermediates for other useful compounds. Manzamine A-F are known from e.g. US4895854 and US4895853 as antitumor cyclic alkaloids derived from extracts of the marine sponge Haliclona sp.

ADVANTAGE - The manzamine compounds are highly effective in inhibiting antigen-driven, immune mediated inflammation and neurogenic inflammation activity, in particular (Ia) which has potent anti-inflammatory activity and low toxicity.

Dwg.0/0

L25 ANSWER 22 OF 24 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-053025 [04] WPIDS
DOC. NO. CPI: C2000-013736
TITLE: Compositions containing sea water and basic amino acid inhibit mastocyte activation and basophile degranulation, useful as anti-allergics and anti-inflammatory agents for the skin, eyes, bronchi and nose.
DERWENT CLASS: B05 D21
INVENTOR(S): BEAUVAIS, F; JOLY, F
PATENT ASSIGNEE(S): (SEPH-N) SEPHRA SARL
COUNTRY COUNT: 51
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9958095	A2	19991118	(200004)*	FR	22
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: BG BR CA CN CZ HU ID IL IN JP KR MX NO NZ PL SG TR US VN YU					
FR 2778562	A1	19991119	(200004)		
EP 1076553	A2	20010221	(200111)	FR	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
KR 2001043619	A	20010525	(200168)		
CN 1309552	A	20010822	(200175)		
BR 9910437	A	20011204	(200203)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9958095	A2	WO 1999-IB862	19990512
FR 2778562	A1	FR 1998-6119	19980514
EP 1076553	A2	EP 1999-918205	19990512
		WO 1999-IB862	19990512
KR 2001043619	A	KR 2000-712774	20001114
CN 1309552	A	CN 1999-808546	19990512
BR 9910437	A	BR 1999-10437	19990512
		WO 1999-IB862	19990512

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 1076553	A2	Based on	WO 9958095
BR 9910437	A	Based on	WO 9958095

PRIORITY APPLN. INFO: FR 1998-6119 19980514

AB WO 9958095 A UPAB: 20000124

NOVELTY - Compositions for pharmaceutical, hygiene, and cosmetic uses containing sea water and a basic amino acid or its salt or ester, or a vegetable and/or animal or phytoplankton extract containing a basic amino acid, together with appropriate inert and non-toxic vehicles or excipients.

DETAILED DESCRIPTION - The basic amino acid may carry a guanidine, (substituted) amine, quaternary ammonium, methyl, carboxamide, cyano, phosphonic or hydrazide group. Vegetable or animal extracts containing an amino acid are preferably those of algae, marine, thermal or lake sediments, bacterial extracts, or plankton extracts. The sea water is filtered and sterilized, and may then be adjusted to isotonia by dilution or deionization. The sea water preferably comprises 30 - 90 (especially 60 - 95) % of the composition and the amino acid is 0.0001 - 10 (especially 0.0005 - 2) % of the composition. In addition, the compositions may contain **antibacterials**, antiparasitics, **antifungals**, anti-pruriginous agents, anti-free radical agents, anesthetics, antivirals, anti-dandruff agents, anti-acneics, anti-seborrheics, hydrocolloid cicatrizing agents, vitamins, pH regulators, aminoglycans and polysaccharides.

ACTIVITY - The effect was studied of sea water and arginine, alone or combined, on the liberation of histamine in vitro. Rat peritoneal mastocytes were suspended in Tyrode solution and pre-incubated in a test solution for 5 minutes at 37 deg. C. The mastocytes were stimulated by **substance P** (5 minutes, 37 deg. C), perchloric acid (0.4N) added and the histamine content measured spectrofluorimetrically. The results are shown in the figure, indicating that in the absence of both sea water and arginine, the percentage histamine liberated was 55% but this dropped when either arginine or sea water were present, reaching around 1 % in the presence of 20% sea water alone or 10% sea water plus 3mM arginine.

MECHANISM OF ACTION - The compositions inhibit the activation of mastocytes, induced by **substance P**, by vasoactive intestinal **peptide**, by calcitonin gene related **peptide** or by bradykinin, and/or they inhibit basophile degranulation.

USE - As anti-allergics and anti-inflammatory agents for the skin, eyes, bronchi and nose.

Dwg.1/1

L25 ANSWER 23 OF 24 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1990-084739 [12] WPIDS
DOC. NO. CPI: C1990-037101
TITLE: **Peptide** formulations for rectal or vaginal admin. - contg. absorption promoter, protease inhibitor and **antibacterial** agent.
DERWENT CLASS: B04 C03
INVENTOR(S): HACKER, E; KOSSOWICZ, J; LOSSE, G; MILDE, K; MUELLER, F; LOESSE, G
PATENT ASSIGNEE(S): (BERC) VEB BERLIN CHEM; (FAFF-N) FAFF EB BERLIN-CHEM; (BERC) VEB BERLIN CHEMIE; (BERC) BERLIN CHEM AG
COUNTRY COUNT: 11
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

DK 8903414	A	19900113 (199012)*		
DD 273980	A	19891206 (199020)B		
EP 371195	A	19900606 (199023)		
R: DE ES FR GB IT SE				
JP 03047114	A	19910228 (199115)		
EP 371195	B1	19930929 (199339)	GE	13
R: DE ES FR GB IT SE				
DE 58905768	G	19931104 (199345)		
DD 273980	B5	19940414 (199420)		
CA 1332349	C	19941011 (199441)		
ES 2059649	T3	19941116 (199501)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DK 8903414	A	DK 1989-3414	19890711
DD 273980	A	DD 1988-317829	19880712
EP 371195	A	EP 1989-112726	19890712
JP 03047114	A	JP 1989-177282	19890711
EP 371195	B1	EP 1989-112726	19890712
DE 58905768	G	DE 1989-505768	19890712
		EP 1989-112726	19890712
DD 273980	B5	DD 1988-317829	19880712
CA 1332349	C	CA 1989-605464	19890712
ES 2059649	T3	EP 1989-112726	19890712

FILING DETAILS:

PATENT NO	KIND		PATENT NO
DE 58905768	G	Based on	EP 371195
ES 2059649	T3	Based on	EP 371195

PRIORITY APPLN. INFO: DD 1988-317829 19880712

AB DK 8903414 A UPAB: 19950110

The biologically active **peptides** are effective over a protracted period, and after fixation to a high molecular carrier, a resorption agent together with a combination of a proteinase inhibitor and an antibiotic.

USE - In medical practice, for the therapy of rectal and vaginal affections.

L25 ANSWER 24 OF 24 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1985-293619 [47] WPIDS
DOC. NO. CPI: C1985-127174
TITLE: Hair tonic compsn. - comprises **peptide** contg. pyroglutamic acid or other aminoacid(s) residue.
DERWENT CLASS: B04 D21
PATENT ASSIGNEE(S): (MEIJ) MEIJI SEIKA KAISHA
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 60202807	A	19851014	(198547)*		3

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 60202807	A	JP 1984-58390	19840328

PRIORITY APPLN. INFO: JP 1984-58390 19840328
AB JP 60202807 A UPAB: 19930925
Hair tonic compsns. comprises **substance P** and **peptide** of the formula I, (where X is pyroglutamic acid residue, (pGlu) or **peptide** or nucleoside comprising 1 to 5 aminoacid residues) or its acid addition salt as active ingredient.

The **substance P** is **peptide** of the formula II.

The **substance P** or **peptide** is used in aq. soln. or suspension. The substance is used in an amt. of 0.005 to 0.02% (wt./vol). The proposed compsn. may additionally contain water, ethanol, oily substance, colouring agent, protecting agent, **antifungi** agent, etc.

USE - The compsn. shows hair growing and hair generation effect.
0/0

```
=> fil reg
FILE 'REGISTRY' ENTERED AT 15:41:53 ON 01 APR 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 American Chemical Society (ACS)

STRUCTURE FILE UPDATES:   31 MAR 2002  HIGHEST RN 403640-18-6
DICTIONARY FILE UPDATES:  31 MAR 2002  HIGHEST RN 403640-18-6

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf
```

claim 10

```
The P indicator for Preparations was not generated for all of the
CAS Registry Numbers that were added to the H/Z/CA/CAplus files between
12/27/01 and 1/23/02.  Use of the P indicator in online and SDI searches
during this period, either directly appended to a CAS Registry Number
or by qualifying an L-number with /P, may have yielded incomplete results.
As of 1/23/02, the situation has been resolved.  Also, note that searches
conducted using the PREP role indicator were not affected.
```

(sequence of claim 5 with at least one "D" amino acid)

```
Customers running searches and/or SDIs in the H/Z/CA/CAplus files
incorporating CAS Registry Numbers with the P indicator between 12/27/01
and 1/23/02, are encouraged to re-run these strategies.  Contact the
CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698,
worldwide, or send an e-mail to help@cas.org for further assistance or to
receive a credit for any duplicate searches.

=> d que l28
L27         1390 SEA FILE=REGISTRY ABB=ON  [HKR]P[HKR]P[-P][-P][FYW][FYW]/SQSP
L28           27 SEA FILE=REGISTRY ABB=ON  L27 AND D/NTE


=> d rn cn sql kwic nte l28 1-27

L28  ANSWER 1 OF 27  REGISTRY  COPYRIGHT 2002 ACS
RN   393563-48-9  REGISTRY
```

= Use Registry # to match sequence to citation

```
CN   Norvalinamide, D-arginyl-L-prolyl-L-lysyl-L-prolyl-D-phenylalanyl-L-
     glutaminyl-D-tryptophyl-L-phenylalanyl-D-tryptophyl-L-leucyl-2-propyl-
     (9CI)  (CA INDEX NAME)
```

sequence length

```
SQL  11
NTE  modified (modifications unspecified)
```

type	location		description
stereo	Arg-1	-	D
stereo	Phe-5	-	D
stereo	Trp-7	-	D
stereo	Trp-9	-	D

```
SEQ      1 RPKPFQWFWL X
           ========
HITS AT:   1-8
```

NTE modified (modifications unspecified)

type	location		description
uncommon	Nva-11	-	-
stereo	Arg-1	-	D
stereo	Phe-5	-	D
stereo	Trp-7	-	D
stereo	Trp-9	-	D

L28 ANSWER 2 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 393563-47-8 REGISTRY
CN Butanamide, D-arginyl-L-prolyl-L-lysyl-L-prolyl-D-phenylalanyl-L-glutaminyl-D-tryptophyl-L-phenylalanyl-D-tryptophyl-L-leucyl-2-amino-2-ethyl- (9CI) (CA INDEX NAME)
SQL 11
NTE modified (modifications unspecified)

type	location		description
stereo	Arg-1	-	D
stereo	Phe-5	-	D
stereo	Trp-7	-	D
stereo	Trp-9	-	D

SEQ 1 RPKPFQWFWL X
========
HITS AT: 1-8
NTE modified (modifications unspecified)

type	location		description
uncommon	Abu-11	-	-
stereo	Arg-1	-	D
stereo	Phe-5	-	D
stereo	Trp-7	-	D
stereo	Trp-9	-	D

L28 ANSWER 3 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 393563-45-6 REGISTRY
CN Cyclohexanecarboxamide, N2-(1-oxooctyl)-D-arginyl-L-prolyl-L-lysyl-L-prolyl-D-phenylalanyl-L-glutaminyl-D-tryptophyl-L-phenylalanyl-D-tryptophyl-L-leucyl-1-amino- (9CI) (CA INDEX NAME)
SQL 11
NTE modified (modifications unspecified)

type	location		description
stereo	Arg-1	-	D
stereo	Phe-5	-	D
stereo	Trp-7	-	D
stereo	Trp-9	-	D

SEQ 1 RPKPFQWFWL X
========
HITS AT: 1-8
NTE modified (modifications unspecified)

type	location		description

uncommon	Aaa-11	-	-
stereo	Arg-1	-	D
stereo	Phe-5	-	D
stereo	Trp-7	-	D
stereo	Trp-9	-	D

L28 ANSWER 4 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 393563-44-5 REGISTRY
CN Cyclohexanecarboxamide, N2-(1-oxobutyl)-D-arginyl-L-prolyl-L-lysyl-L-prolyl-D-phenylalanyl-L-glutaminyl-D-tryptophyl-L-phenylalanyl-D-tryptophyl-L-leucyl-1-amino- (9CI) (CA INDEX NAME)
SQL 11
NTE modified (modifications unspecified)

type	location		description
stereo	Arg-1	-	D
stereo	Phe-5	-	D
stereo	Trp-7	-	D
stereo	Trp-9	-	D

SEQ 1 RPKPFQWFWL X
========
HITS AT: 1-8
NTE modified (modifications unspecified)

type	location		description
uncommon	Aaa-11	-	-
stereo	Arg-1	-	D
stereo	Phe-5	-	D
stereo	Trp-7	-	D
stereo	Trp-9	-	D

L28 ANSWER 5 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 393563-43-4 REGISTRY
CN Cyclohexanecarboxamide, D-arginyl-L-prolyl-L-lysyl-L-prolyl-D-phenylalanyl-L-glutaminyl-D-tryptophyl-L-phenylalanyl-D-tryptophyl-L-leucyl-1-amino- (9CI) (CA INDEX NAME)
SQL 11
NTE modified (modifications unspecified)

type	location		description
stereo	Arg-1	-	D
stereo	Phe-5	-	D
stereo	Trp-7	-	D
stereo	Trp-9	-	D

SEQ 1 RPKPFQWFWL X
========
HITS AT: 1-8
NTE modified (modifications unspecified)

type	location		description
uncommon	Aaa-11	-	-
stereo	Arg-1	-	D

stereo	Phe-5	-	D
stereo	Trp-7	-	D
stereo	Trp-9	-	D

L28 ANSWER 6 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 250374-98-2 REGISTRY
CN L-Methioninamide, L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-L-phenylalanyl-4-(4-hydroxybenzoyl)-D-phenylalanylglycyl-L-leucyl- (9CI) (CA INDEX NAME)
SQL 11
NTE modified (modifications unspecified)

type	------ location ------		description
stereo	Phe-8	-	D

SEQ 1 RPKPQQFFGL M
========
HITS AT: 1-8
NTE modified (modifications unspecified)

type	------ location ------		description
stereo	Phe-8	-	D

L28 ANSWER 7 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 211191-18-3 REGISTRY
CN L-Tryptophanamide, N2-[5-[[5-[(3aS,4S,6aR)-hexahydro-5,5-dioxido-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-1-oxopentyl]-L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-L-phenylalanyl-L-phenylalanyl-D-prolyl-4-benzoyl-N-methyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
SQL 12
NTE modified (modifications unspecified)

type	------ location ------		description
stereo	Phe-10	-	D

SEQ 1 XRPKPQQFFP FW
========
HITS AT: 2-9
NTE modified (modifications unspecified)

type	------ location ------		description
uncommon	Oaa-1	-	-
stereo	Phe-10	-	D

L28 ANSWER 8 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 151910-82-6 REGISTRY
CN Substance P, 1-D-arginine-5-(ar-fluoro-D-phenylalanine)-7-D-tryptophan-8-(ar-fluoro-D-tryptophan)-11-L-leucinamide- (9CI) (CA INDEX NAME)
SQL 11
NTE modified

type	------ location ------		description

stereo	Arg-1	-	D
stereo	Phe-5	-	D
stereo	Trp-7	-	D
stereo	Trp-8	-	D

SEQ 1 RPKPFQWWGL L
========
HITS AT: 1-8
NTE modified

type	------ location ------		description
terminal mod.	Leu-11	-	C-terminal amide
stereo	Arg-1	-	D
stereo	Phe-5	-	D
stereo	Trp-7	-	D
stereo	Trp-8	-	D

L28 ANSWER 9 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 151839-23-5 REGISTRY
CN Substance P, 1-D-arginine-5-(ar-fluoro-D-phenylalanine)-7-(ar-fluoro-D-tryptophan)-8-D-tryptophan-11-L-leucinamide- (9CI) (CA INDEX NAME)
SQL 11
NTE modified

type	------ location ------		description
stereo	Arg-1	-	D
stereo	Phe-5	-	D
stereo	Trp-7	-	D
stereo	Trp-8	-	D

SEQ 1 RPKPFQWWGL L
========
HITS AT: 1-8
NTE modified

type	------ location ------		description
terminal mod.	Leu-11	-	C-terminal amide
stereo	Arg-1	-	D
stereo	Phe-5	-	D
stereo	Trp-7	-	D
stereo	Trp-8	-	D

L28 ANSWER 10 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 151839-22-4 REGISTRY
CN Substance P, 1-D-arginine-5-(ar-fluoro-D-phenylalanine)-7-D-tryptophan-8-D-tryptophan-11-L-leucinamide- (9CI) (CA INDEX NAME)
SQL 11
NTE modified

type	------ location ------		description
stereo	Arg-1	-	D
stereo	Phe-5	-	D
stereo	Trp-7	-	D
stereo	Trp-8	-	D

```
SEQ      1 RPKPFQWWGL L
           --------===
HITS AT:   1-8
NTE  modified
-------------------------------------------------------------------------
 type            ------ location ------         description
-------------------------------------------------------------------------
terminal mod.    Leu-11          -         C-terminal amide
stereo           Arg-1           -         D
stereo           Phe-5           -         D
stereo           Trp-7           -         D
stereo           Trp-8           -         D
-------------------------------------------------------------------------

L28  ANSWER 11 OF 27  REGISTRY  COPYRIGHT 2002 ACS
RN   145996-27-6  REGISTRY
CN   L-Norleucinamide, D-arginyl-D-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-
     asparaginyl-D-phenylalanyl-L-phenylalanyl-N6-[6-(3-mercapto-2,5-dioxo-1-
     pyrrolidinyl)-1-oxohexyl]-L-lysyl-L-leucyl-, (9.fwdarw.7')-thioether with
     D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-L-phenylalanyl-
     L-cysteinyl-D-phenylalanyl-L-leucyl-L-arginine (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   L-Norleucinamide, D-arginyl-D-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-
     asparaginyl-D-phenylalanyl-L-phenylalanyl-N6-[6-(3-mercapto-2,5-dioxo-1-
     pyrrolidinyl)-1-oxohexyl]-L-lysyl-L-leucyl-, (9.fwdarw.7')-sulfide with
     D-arginyl-L-arginyl-L-prolyl-trans-4-hydroxy-L-prolylglycyl-L-phenylalanyl-
     L-cysteinyl-D-phenylalanyl-L-leucyl-L-arginine
SQL  21,11,10
NTE  multichain
     modified (modifications unspecified)
-------------------------------------------------------------------------
 type            ------ location ------         description
-------------------------------------------------------------------------
stereo           Arg-1           -         D
stereo           Pro-2           -         D
stereo           Phe-7           -         D
stereo           Arg-1'          -         D
stereo           Phe-8'          -         D
-------------------------------------------------------------------------

SEQ      1 RPKPQNFFKL X
           ========
HITS AT:   1-8

NTE  multichain
     modified (modifications unspecified)
-------------------------------------------------------------------------
 type            ------ location ------         description
-------------------------------------------------------------------------
bridge           Lys-9       - Cys-7'      covalent bridge
uncommon         Nle-11          -         -
uncommon         Hyp-4'          -         -
stereo           Arg-1           -         D
stereo           Pro-2           -         D
stereo           Phe-7           -         D
stereo           Arg-1'          -         D
stereo           Phe-8'          -         D
-------------------------------------------------------------------------

L28  ANSWER 12 OF 27  REGISTRY  COPYRIGHT 2002 ACS
RN   145996-24-3  REGISTRY
CN   L-Norleucinamide, D-arginyl-D-prolyl-L-lysyl-L-prolyl-L-glutaminyl-N6-[6-
```

(3-mercapto-2,5-dioxo-1-pyrrolidinyl)-1-oxohexyl]-L-lysyl-D-phenylalanyl-L-phenylalanyl-D-tryptophyl-L-leucyl-, (6.fwdarw.7')-thioether with D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-L-phenylalanyl-L-cysteinyl-D-phenylalanyl-L-leucyl-L-arginine (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN L-Norleucinamide, D-arginyl-D-prolyl-L-lysyl-L-prolyl-L-glutaminyl-N6-[6-(3-mercapto-2,5-dioxo-1-pyrrolidinyl)-1-oxohexyl]-L-lysyl-D-phenylalanyl-L-phenylalanyl-D-tryptophyl-L-leucyl-, (6.fwdarw.7')-sulfide with D-arginyl-L-arginyl-L-prolyl-trans-4-hydroxy-L-prolylglycyl-L-phenylalanyl-L-cysteinyl-D-phenylalanyl-L-leucyl-L-arginine

SQL 21,11,10

NTE multichain
modified (modifications unspecified)

type	------ location ------		description
stereo	Arg-1	-	D
stereo	Pro-2	-	D
stereo	Phe-7	-	D
stereo	Trp-9	-	D
stereo	Arg-1'	-	D
stereo	Phe-8'	-	D

SEQ 1 RPKPQKFFWL X
========
HITS AT: 1-8

NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Lys-6	- Cys-7'	covalent bridge
uncommon	Nle-11	-	-
uncommon	Hyp-4'	-	-
stereo	Arg-1	-	D
stereo	Pro-2	-	D
stereo	Phe-7	-	D
stereo	Trp-9	-	D
stereo	Arg-1'	-	D
stereo	Phe-8'	-	D

L28 ANSWER 13 OF 27 REGISTRY COPYRIGHT 2002 ACS

RN 145996-23-2 REGISTRY

CN L-Norleucinamide, D-arginyl-D-prolyl-L-lysyl-L-prolyl-N6-[6-(3-mercapto-2,5-dioxo-1-pyrrolidinyl)-1-oxohexyl]-L-lysyl-L-asparaginyl-D-phenylalanyl-L-phenylalanyl-D-tryptophyl-L-leucyl-, (5.fwdarw.7')-thioether with D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-L-phenylalanyl-L-cysteinyl-D-phenylalanyl-L-leucyl-L-arginine (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN L-Norleucinamide, D-arginyl-D-prolyl-L-lysyl-L-prolyl-N6-[6-(3-mercapto-2,5-dioxo-1-pyrrolidinyl)-1-oxohexyl]-L-lysyl-L-asparaginyl-D-phenylalanyl-L-phenylalanyl-D-tryptophyl-L-leucyl-, (5.fwdarw.7')-sulfide with D-arginyl-L-arginyl-L-prolyl-trans-4-hydroxy-L-prolylglycyl-L-phenylalanyl-L-cysteinyl-D-phenylalanyl-L-leucyl-L-arginine

SQL 21,11,10

NTE multichain
modified (modifications unspecified)

type	------ location ------		description

stereo	Arg-1	-	D
stereo	Pro-2	-	D
stereo	Phe-7	-	D
stereo	Trp-9	-	D
stereo	Arg-1'	-	D
stereo	Phe-8'	-	D

SEQ 1 RPKPKNFFWL X
========
HITS AT: 1-8

NTE multichain
modified (modifications unspecified)

type	location		description
bridge	Lys-5	- Cys-7'	covalent bridge
uncommon	Nle-11	-	-
uncommon	Hyp-4'	-	-
stereo	Arg-1	-	D
stereo	Pro-2	-	D
stereo	Phe-7	-	D
stereo	Trp-9	-	D
stereo	Arg-1'	-	D
stereo	Phe-8'	-	D

L28 ANSWER 14 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 145996-22-1 REGISTRY
CN L-Norleucinamide, D-arginyl-D-prolyl-N6-[6-(3-mercapto-2,5-dioxo-1-pyrrolidinyl)-1-oxohexyl]-L-lysyl-L-prolyl-L-glutaminyl-L-asparaginyl-D-phenylalanyl-L-phenylalanyl-D-tryptophyl-L-leucyl-, (3.fwdarw.7')-thioether with D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-L-phenylalanyl-L-cysteinyl-D-phenylalanyl-L-leucyl-L-arginine (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Norleucinamide, D-arginyl-D-prolyl-N6-[6-(3-mercapto-2,5-dioxo-1-pyrrolidinyl)-1-oxohexyl]-L-lysyl-L-prolyl-L-glutaminyl-L-asparaginyl-D-phenylalanyl-L-phenylalanyl-D-tryptophyl-L-leucyl-, (3.fwdarw.7')-sulfide with D-arginyl-L-arginyl-L-prolyl-trans-4-hydroxy-L-prolylglycyl-L-phenylalanyl-L-cysteinyl-D-phenylalanyl-L-leucyl-L-arginine
SQL 21,11,10
NTE multichain
modified (modifications unspecified)

type	location		description
stereo	Arg-1	-	D
stereo	Pro-2	-	D
stereo	Phe-7	-	D
stereo	Trp-9	-	D
stereo	Arg-1'	-	D
stereo	Phe-8'	-	D

SEQ 1 RPKPQNFFWL X
========
HITS AT: 1-8

NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Lys-3	- Cys-7'	covalent bridge
uncommon	Nle-11	-	-
uncommon	Hyp-4'	-	-
stereo	Arg-1	-	D
stereo	Pro-2	-	D
stereo	Phe-7	-	D
stereo	Trp-9	-	D
stereo	Arg-1'	-	D
stereo	Phe-8'	-	D

L28 ANSWER 15 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 145996-20-9 REGISTRY
CN L-Norleucinamide, N6-[6-(3-mercapto-2,5-dioxo-1-pyrrolidinyl)-1-oxohexyl]-L-lysyl-D-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-asparaginyl-D-phenylalanyl-L-phenylalanyl-D-tryptophyl-L-leucyl-, (1.fwdarw.7')-thioether with D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-L-phenylalanyl-L-cysteinyl-D-phenylalanyl-L-leucyl-L-arginine (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Norleucinamide, N6-[6-(3-mercapto-2,5-dioxo-1-pyrrolidinyl)-1-oxohexyl]-L-lysyl-D-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-asparaginyl-D-phenylalanyl-L-phenylalanyl-D-tryptophyl-L-leucyl-, (1.fwdarw.7')-sulfide with D-arginyl-L-arginyl-L-prolyl-trans-4-hydroxy-L-prolylglycyl-L-phenylalanyl-L-cysteinyl-D-phenylalanyl-L-leucyl-L-arginine
SQL 21,11,10
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
stereo	Pro-2	-	D
stereo	Phe-7	-	D
stereo	Trp-9	-	D
stereo	Arg-1'	-	D
stereo	Phe-8'	-	D

SEQ 1 KPKPQNFFWL X
========
HITS AT: 1-8

NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Lys-1	- Cys-7'	covalent bridge
uncommon	Nle-11	-	-
uncommon	Hyp-4'	-	-
stereo	Pro-2	-	D
stereo	Phe-7	-	D
stereo	Trp-9	-	D
stereo	Arg-1'	-	D
stereo	Phe-8'	-	D

L28 ANSWER 16 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 145964-84-7 REGISTRY
CN L-Lysinamide, D-arginyl-D-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-asparaginyl-D-phenylalanyl-L-phenylalanyl-D-tryptophyl-L-leucyl-N6-[6-(3-

mercapto-2,5-dioxo-1-pyrrolidinyl)-1-oxohexyl]-, (11.fwdarw.7')-thioether with D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-L-phenylalanyl-L-cysteinyl-D-phenylalanyl-L-leucyl-L-arginine (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN L-Lysinamide, D-arginyl-D-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-asparaginyl-D-phenylalanyl-L-phenylalanyl-D-tryptophyl-L-leucyl-N6-[6-(3-mercapto-2,5-dioxo-1-pyrrolidinyl)-1-oxohexyl]-, (11.fwdarw.7')-sulfide with D-arginyl-L-arginyl-L-prolyl-trans-4-hydroxy-L-prolylglycyl-L-phenylalanyl-L-cysteinyl-D-phenylalanyl-L-leucyl-L-arginine

SQL 21,11,10

NTE multichain
modified (modifications unspecified)

type	------ location ------		description
stereo	Arg-1	-	D
stereo	Pro-2	-	D
stereo	Phe-7	-	D
stereo	Trp-9	-	D
stereo	Arg-1'	-	D
stereo	Phe-8'	-	D

SEQ 1 RPKPQNFFWL K
========
HITS AT: 1-8

NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Lys-11	- Cys-7'	covalent bridge
uncommon	Hyp-4'	-	-
stereo	Arg-1	-	D
stereo	Pro-2	-	D
stereo	Phe-7	-	D
stereo	Trp-9	-	D
stereo	Arg-1'	-	D
stereo	Phe-8'	-	D

L28 ANSWER 17 OF 27 REGISTRY COPYRIGHT 2002 ACS

RN 145964-83-6 REGISTRY

CN L-Norleucinamide, D-arginyl-D-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-asparaginyl-D-phenylalanyl-L-phenylalanyl-D-tryptophyl-N6-[6-(3-mercapto-2,5-dioxo-1-pyrrolidinyl)-1-oxohexyl]-L-lysyl-, (10.fwdarw.7')-thioether with D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-L-phenylalanyl-L-cysteinyl-D-phenylalanyl-L-leucyl-L-arginine (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN L-Norleucinamide, D-arginyl-D-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-asparaginyl-D-phenylalanyl-L-phenylalanyl-D-tryptophyl-N6-[6-(3-mercapto-2,5-dioxo-1-pyrrolidinyl)-1-oxohexyl]-L-lysyl-, (10.fwdarw.7')-sulfide with D-arginyl-L-arginyl-L-prolyl-trans-4-hydroxy-L-prolylglycyl-L-phenylalanyl-L-cysteinyl-D-phenylalanyl-L-leucyl-L-arginine

SQL 21,11,10

NTE multichain
homopolymer

type	------ location ------	description

stereo	Arg-1	-	D
stereo	Pro-2	-	D
stereo	Phe-7	-	D
stereo	Trp-9	-	D

SEQ 1 RPKPQNFFWK X
========
HITS AT: 1-8

NTE multichain
homopolymer

type	location		description
bridge	Lys-10	- Cys-7'	covalent bridge
uncommon	Nle-11	-	-
uncommon	Hyp-4'	-	-
stereo	Arg-1	-	D
stereo	Pro-2	-	D
stereo	Phe-7	-	D
stereo	Trp-9	-	D

L28 ANSWER 18 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 111139-27-6 REGISTRY
CN Substance P, 5-(6-oxo-L-lysine)-6-(6-oxo-D-lysine)- (9CI) (CA INDEX NAME)
SQL 11
NTE modified

type	location		description
stereo	Lys-6	-	D

SEQ 1 RPKPKKFFGL M
========
HITS AT: 1-8
NTE modified

type	location		description
stereo	Lys-6	-	D

L28 ANSWER 19 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 110072-71-4 REGISTRY
CN Substance P, 5-(6-oxo-D-lysine)-6-(6-oxo-D-lysine)- (9CI) (CA INDEX NAME)
SQL 11
NTE modified

type	location		description
stereo	Lys-5	-	D
stereo	Lys-6	-	D

SEQ 1 RPKPKKFFGL M
========
HITS AT: 1-8
NTE modified

type	location		description

stereo	Lys-5	-	D
stereo	Lys-6	-	D

L28 ANSWER 20 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 110072-70-3 REGISTRY
CN Substance P, 6-(6-oxo-D-lysine)- (9CI) (CA INDEX NAME)
SQL 11
NTE modified

type	------ location ------		description
stereo	Lys-6	-	D

SEQ 1 RPKPQKFFGL M
========
HITS AT: 1-8
NTE modified

type	------ location ------		description
stereo	Lys-6	-	D

L28 ANSWER 21 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 110072-69-0 REGISTRY
CN Substance P, 5-(6-oxo-D-lysine)- (9CI) (CA INDEX NAME)
SQL 11
NTE modified

type	------ location ------		description
stereo	Lys-5	-	D

SEQ 1 RPKPKQFFGL M
========
HITS AT: 1-8
NTE modified

type	------ location ------		description
stereo	Lys-5	-	D

L28 ANSWER 22 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 102966-11-0 REGISTRY
CN D-Phenylalaninamide, N2-[(phenylmethoxy)carbonyl]-L-arginyl-D-prolyl-L-lysyl-D-prolyl-L-glutaminyl-L-glutaminyl-D-phenylalanyl-N-[2-[[1-[[[1-(methoxycarbonyl)-3-(methylthio)propyl]amino]carbonyl]-3-methylbutyl]thio]ethyl]-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)
SQL 11
NTE modified (modifications unspecified)

type	------ location ------		description
stereo	Pro-2	-	D
stereo	Pro-4	-	D
stereo	Phe-7	-	D
stereo	Phe-8	-	D
stereo	Met-11	-	D

SEQ 1 RPKPQQFFGI M
========
HITS AT: 1-8
NTE modified (modifications unspecified)

type	location		description
stereo	Pro-2	-	D
stereo	Pro-4	-	D
stereo	Phe-7	-	D
stereo	Phe-8	-	D
stereo	Met-11	-	D
replacement	Ile-10	-	thia

L28 ANSWER 23 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 101915-12-2 REGISTRY
CN D-Phenylalaninamide, L-arginyl-D-prolyl-L-lysyl-D-prolyl-L-glutaminyl-L-glutaminyl-D-phenylalanyl-N-[2-[[1-[[[1-(methoxycarbonyl)-3-(methylthio)propyl]amino]carbonyl]-3-methylbutyl]thio]ethyl]-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)
SQL 11
NTE modified

type	location		description
stereo	Pro-2	-	D
stereo	Pro-4	-	D
stereo	Phe-7	-	D
stereo	Phe-8	-	D
stereo	Leu-10	-	D
stereo	Met-11	-	D

SEQ 1 RPKPQQFFGL M
========
HITS AT: 1-8
NTE modified

type	location		description
stereo	Pro-2	-	D
stereo	Pro-4	-	D
stereo	Phe-7	-	D
stereo	Phe-8	-	D
stereo	Leu-10	-	D
stereo	Met-11	-	D
replacement	Leu-10	-	thia

L28 ANSWER 24 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 101915-11-1 REGISTRY
CN D-Phenylalaninamide, N2-[(phenylmethoxy)carbonyl]-L-arginyl-D-prolyl-N6-[(phenylmethoxy)carbonyl]-L-lysyl-D-prolyl-L-glutaminyl-L-glutaminyl-D-phenylalanyl-N-[2-[[1-[[[1-(methoxycarbonyl)-3-(methylthio)propyl]amino]carbonyl]-3-methylbutyl]thio]ethyl]-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)
SQL 11
NTE modified

type	location		description

stereo	Pro-2	-	D
stereo	Pro-4	-	D
stereo	Phe-7	-	D
stereo	Phe-8	-	D
stereo	Leu-10	-	D
stereo	Met-11	-	D

SEQ 1 RPKPQQFFGL M
========
HITS AT: 1-8
NTE modified

type	------ location ------		description
stereo	Pro-2	-	D
stereo	Pro-4	-	D
stereo	Phe-7	-	D
stereo	Phe-8	-	D
stereo	Leu-10	-	D
stereo	Met-11	-	D
replacement	Leu-10	-	thia

L28 ANSWER 25 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 101835-76-1 REGISTRY
CN D-Phenylalaninamide, N2-[(phenylmethoxy)carbonyl]-L-arginyl-D-prolyl-N6-[(phenylmethoxy)carbonyl]-L-lysyl-L-prolyl-L-asparaginyl-L-arginyl-D-phenylalanyl-N-[2-[[1-[[[1-(methoxycarbonyl)-3-(methylthio)propyl]amino]carbonyl]-3-methylbutyl]thio]ethyl]-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)
SQL 11
NTE modified

type	------ location ------		description
stereo	Pro-2	-	D
stereo	Phe-7	-	D
stereo	Phe-8	-	D
stereo	Leu-10	-	D
stereo	Met-11	-	D

SEQ 1 RPKPNRFFGL M
========
HITS AT: 1-8
NTE modified

type	------ location ------		description
stereo	Pro-2	-	D
stereo	Phe-7	-	D
stereo	Phe-8	-	D
stereo	Leu-10	-	D
stereo	Met-11	-	D
replacement	Leu-10	-	thia

L28 ANSWER 26 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 101835-74-9 REGISTRY
CN D-Phenylalaninamide, L-arginyl-D-prolyl-L-lysyl-D-prolyl-L-glutaminyl-L-glutaminyl-D-phenylalanyl-N-[2-[[1-[[[1-(methoxycarbonyl)-3-

(methylthio)propyl]amino]carbonyl]-3-methylbutyl]thio]ethyl]-,
[S-(R*,S*)]- (9CI) (CA INDEX NAME)
SQL 11
NTE modified

type	location		description
stereo	Pro-2	-	D
stereo	Pro-4	-	D
stereo	Phe-7	-	D
stereo	Phe-8	-	D
stereo	Met-11	-	D

SEQ 1 RPKPQQFFGL M
========
HITS AT: 1-8
NTE modified

type	location		description
stereo	Pro-2	-	D
stereo	Pro-4	-	D
stereo	Phe-7	-	D
stereo	Phe-8	-	D
stereo	Met-11	-	D
replacement	Leu-10	-	thia

L28 ANSWER 27 OF 27 REGISTRY COPYRIGHT 2002 ACS
RN 101835-73-8 REGISTRY
CN D-Phenylalaninamide, N2-[(phenylmethoxy)carbonyl]-L-arginyl-D-prolyl-N6-
[(phenylmethoxy)carbonyl]-L-lysyl-D-prolyl-L-glutaminyl-L-glutaminyl-D-
phenylalanyl-N-[2-[[1-[[[1-(methoxycarbonyl)-3-
(methylthio)propyl]amino]carbonyl]-3-methylbutyl]thio]ethyl]-,
[S-(R*,S*)]- (9CI) (CA INDEX NAME)
SQL 11
NTE modified

type	location		description
stereo	Pro-2	-	D
stereo	Pro-4	-	D
stereo	Phe-7	-	D
stereo	Phe-8	-	D
stereo	Met-11	-	D

SEQ 1 RPKPQQFFGL M
========
HITS AT: 1-8
NTE modified

type	location		description
stereo	Pro-2	-	D
stereo	Pro-4	-	D
stereo	Phe-7	-	D
stereo	Phe-8	-	D
stereo	Met-11	-	D
replacement	Leu-10	-	thia

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=> fil capl; s l28
FILE 'CAPLUS' ENTERED AT 15:42:36 ON 01 APR 2002
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FILE COVERS 1907 - 1 Apr 2002 VOL 136 ISS 14
FILE LAST UPDATED: 30 Mar 2002 (20020330/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

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L29         10 L28

=> d ibib ab hitrn l29 1-10; fil hom

L29  ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:107370  CAPLUS
DOCUMENT NUMBER:          136:151442
TITLE:                    Preparation of substance P analogs for the treatment
                          of cancer
INVENTOR(S):              Burman, Anand C.; Prasad, Sudhanand; Mukherhee, Rama;
                          Jaggi, Manu; Singh, Anu T.
PATENT ASSIGNEE(S):       Dabur Research Foundation, India; Cord, Janet,I.
SOURCE:                   PCT Int. Appl., 45 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2002010194      A1   20020207       WO 2000-US20875  20000731
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
```

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
OTHER SOURCE(S): MARPAT 136:151442
AB The invention encompasses novel synthetic peptide analogs that are antagonists to substance P, substance P-like peptides and related peptides that are useful for the treatment of cancer. The invention particularly relates to peptides, e.g, X-D-Arg-Pro-Lys-Pro-D-Phe-Gln-D-Trp-Phe-D-Trp-Leu-R-NH2 [I; X is acetyl or a straight, branched, or cyclic alkanoyl group having 3-18 carbon atoms, or is deleted; R is .alpha.-aminoisobutyric acid, .alpha.,.alpha.-diethyl- or .alpha.,.alpha.-dipropylglycine, 1-aminocyclopentanecarboxylic acid (Ac5c) or 1-aminocyclohexanecarboxylic acid or a hydrolyzable carboxy protecting group] or D-Phe-Gln-D-Trp-Phe-D-Trp-Leu-R-NH2 or pharmaceutically acceptable salts which incorporate .alpha.,.alpha.-dialkylated amino acids in a site-specific manner. Thus, I (X = butanoyl, R = Ac5c) was prepd. by the solid-phase method using a Rink Amide resin and showed significant antitumor activity on human colon adenocarcinoma xenografts (78.54% inhibition after 21 days).
IT **393563-43-4P 393563-44-5P 393563-45-6P 393563-47-8P 393563-48-9P** > use Registry numbers to match citation to sequence
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substance P analogs for the treatment of cancer)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:733868 CAPLUS
DOCUMENT NUMBER: 131:348788
TITLE: Photolabeling reagent containing (p-hydroxylbenzoyl)phenylalanine
INVENTOR(S): Maggio, John E.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: U.S., 18 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5986136	A	19991116	US 1998-57799	19980409

PRIORITY APPLN. INFO.: US 1997-43019P P 19970415
OTHER SOURCE(S): MARPAT 131:348788
AB Disclosed is (p-hydroxylbenzoyl)phenylalanine compd. I (X = H, amine protecting group; OY = OH, activating group for carboxylic acid, or protecting group for carboxylic acid; Z = H or phenolic protecting group, with the proviso that Z is not a straight chained, unsatd. alkyl group such as, for example, Me or Et, and at least one of X, Y or Z is not H). Also disclosed is a photoreactive polypeptide having a polypeptide chain comprising a residue of the compd. described above. Also disclosed is a method of labeling a target mol. which forms a complex with the photoreactive polypolypeptide by photolyzing the photoreactive polypeptide when complexed with the target mol. Fmoc-protected p-(4-hydroxybenzoyl)phenylalanine was prepd. and used in the synthesis of substance P analogs. The analogs were radiolabeled with 125I and used in binding studies.
IT **250374-98-2P**

RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(photolabeling reagent contg. (p-hydroxylbenzoyl)phenylalanine)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:401965 CAPLUS
DOCUMENT NUMBER: 129:161835
TITLE: Asymmetric synthesis of Boc-N-methyl-p-benzoylphenylalanine. Preparation of a photoreactive antagonist of substance P
AUTHOR(S): Karoyan, Philippe; Sagan, Sandrine; Clodic, Gil; Lavielle, Solange; Chassaing, Gerard
CORPORATE SOURCE: Laboratoire de Chimie Organique Biologique Associe au CNRS, Universite P. et M. Curie, UMR 7613, Paris, 75252, Fr.
SOURCE: Bioorg. Med. Chem. Lett. (1998), 8(11), 1369-1374
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The asym. synthesis of (S)-Boc-N-methyl-p-benzoylphenylalanine was performed by the alkylation of Boc-sarcosine camphorsultam deriv. I with p-benzoylbenzyl bromide. N-methyl-p-benzoylphenylalanine, a photoreactive amino acid, was then incorporated into the sequence of a Substance P peptide antagonist, Bapa-[D-Pro9, MePhe(pBz)10, Trp11]SP (II; Bapa = biotine-sulfone-aminopentanoyl). Comparison of the affinity and antagonistic properties of peptide II for human tachykinin NK-1 receptor demonstrated that this photoreactive antagonist should be a suitable tool for photolabeling studies.
IT **211191-18-3P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(asym. synthesis of Boc-N-methyl-p-benzoylphenylalanine and its incorporation into a photoreactive peptide antagonist of substance P)

L29 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:596420 CAPLUS
DOCUMENT NUMBER: 121:196420
TITLE: Effects of neuropeptide analogs on calcium flux and proliferation in lung cancer cell lines
AUTHOR(S): Bunn, Paul A., Jr.; Chan, Daniel; Stewart, John; Gera, Lajos; Tolley, Russell; Jewett, Philip; Tagawa, Maureen; Alford, Charlotte; Mochzuki, Tohru; Yanaihara, Noboru
CORPORATE SOURCE: Cancer Cent., Univ. Colorado, Denver, CO, 80262, USA
SOURCE: Cancer Res. (1994), 54(13), 3602-10
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Small cell lung cancers (SCLC) and some non-small cell lung cancers (NSCLC) have neuroendocrine features which include prodn. of a variety of neuropeptides, cell surface expression of the receptors for these peptides, and autocrine stimulation by the peptides. Previous studies showed that some peptide antagonists and anti-peptide antibodies inhibited the growth of SCLC cell lines which expressed receptors for the specific peptide. The authors and others showed that the heterogeneity of peptide receptor expression and responsiveness was a major potential obstacle for developing therapeutic uses of peptide antagonists. In this manuscript the authors evaluated the effects of 11 peptide antagonists (3 bombesin-specific, 2 cholecystokinin-specific, 1 arginine vasopressin

(AVP)-specific, and 5 substance P derivs. with broad specificity) on peptide-induced calcium mobilization and growth of SCLC and NSCLC cell lines. For each antagonist, the authors detd. the dose-response effects, specificity of peptide antagonism, and biol. stability in serum using Indo-1AM-based flow cytometric assays. The authors found that the three bombesin antagonists, S30, SC196, and L336,175, varied in potency from 10 nM to 10 .mu.M, varied in serum stability from 6 h to more than 24 h, and had no effect on the calcium response elicited by other peptides. None of these compds. effectively inhibited the growth of SCLC cell lines in [3H]dThd and cell growth assays in vitro. Similarly, the three cholecystokinin and AVP antagonists were highly specific for cholecystokinin and AVP, resp., had widely varying potency, but had little inhibitory effect on SCLC growth in vitro. In contrast, the five substance P derivs. inhibited the calcium response to bombesin, AVP, bradykinin, and fetal bovine serum. None of these five antagonists were as potent as the six specific antagonists described above, but they were more effective in inhibiting the growth of SCLC cell lines in vitro. These substance P derivs. inhibited the growth of peptide-sensitive SCLC cell lines more efficiently than their inhibition of peptide-insensitive NSCLC or breast cancer cell lines. Relatively high concns. of these substance P derivs. were required to inhibit in vitro growth, even in the absence of added peptide. It is likely that more potent broad spectrum antagonists, toxins, or radio-labeled stable antagonists will need to be developed for maximal clin. development of this type of anti-growth factor therapy.

IT **151910-82-6**
RL: BIOL (Biological study)
(calcium mobilization and cell proliferation inhibition by, in human cancer cells)

L29 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:23722 CAPLUS
DOCUMENT NUMBER: 120:23722
TITLE: Novel substance P analogs inhibit circular muscle contraction of guinea pig ileum and depolarization of newborn rat spinal cord induced by substance P
AUTHOR(S): Mochizuki, Tohru; Ohshima, Keiichi; Kuwahara, Atukazu; Yanagisawa, Mitushiko; Otsuka, Masanori; Yanaihara, Noboru
CORPORATE SOURCE: Sch. Pharm. Sci., Univ. Shizuoka, Shizuoka, 422, Japan
SOURCE: Regul. Pept. (1993), 46(1-2), 321-5
CODEN: REPPDY; ISSN: 0167-0115
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ten synthetic substance P (SP) analogs were investigated as antagonists of contractions of guinea pig ileum circular muscle induced by SP, neurokinin A, and neurokinin B and of elec. stimulation and depolarization of newborn rat spinal cord induced by SP. Both [D-Arg1,Leu3,D-Phe5,D-Trp7,9,Ala11]SP and [D-Arg1,Leu3,D-Phe(F)5,D-Trp7,9,Ala11]SP decreased the contraction of the guinea pig ileum induced by SP, but not the contractions induced by the neurokinins. In the newborn rat spinal cord prepn. these 2 analogs also inhibited SP-induced depolarization. The other 8 analogs showed no effect or weak agonistic effect in both bioassay systems.

IT **151839-22-4 151839-23-5 151910-82-6**
RL: BIOL (Biological study)
(substance P effect on ileum contraction and spinal cord depolarization response to)

L29 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:117549 CAPLUS
DOCUMENT NUMBER: 118:117549
TITLE: Bradykinin antagonists
INVENTOR(S): Cheronis, John C.; Blodgett, James K.; Whalley, Eric

T.; Eubanks, Shadrach R.; Allen, Lisa Gay; Nguyen Khe Thanh
PATENT ASSIGNEE(S): Cortech, Inc., USA
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9217201	A1	19921015	WO 1992-US2431	19920330
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
CA 2106677	AA	19921002	CA 1992-2106677	19920330
AU 9218751	A1	19921102	AU 1992-18751	19920330
AU 660683	B2	19950706		
EP 586613	A1	19940316	EP 1992-917400	19920330
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
HU 65328	A2	19940502	HU 1993-2780	19920330
JP 06508116	T2	19940914	JP 1992-510219	19920330
US 5416191	A	19950516	US 1993-2684	19930108
NO 9303508	A	19930930	NO 1993-3508	19930930
US 5620958	A	19970415	US 1994-227184	19940413
US 5635593	A	19970603	US 1995-440352	19950512

PRIORITY APPLN. INFO.: US 1991-677391 A 19910401
US 1992-859582 A 19920327
WO 1992-US2431 A 19920330
US 1994-227184 A1 19940413

OTHER SOURCE(S): MARPAT 118:117549

AB Bradykinin antagonists are modified for increased potency and/or duration of action. The modification is done by joining a bradykinin (BK1) receptor antagonist with a BK2 antagonist or (.mu.-)opioid receptor agonist or a neuropeptide receptor antagonist through a linker, such as a bissuccinimidoalkane. CP-0127 (I) was prepd. by dimerized the monomer peptide CP-0126 in bismaleimidohexane. I (9 nmol/kg/min; i.v.) totally inhibited in the rat the blood pressure response to bradykinin (4 .times. 10-9 mol), whereas the parent peptide showed little activity.

IT **145964-83-6P 145964-84-7P 145996-20-9P**
145996-22-1P 145996-23-2P 145996-24-3P
145996-27-6P
RL: PREP (Preparation)
(prepn. of, as bradykinin antagonists)

L29 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:598903 CAPLUS
DOCUMENT NUMBER: 107:198903
TITLE: Syntheses and biological activities of substance P analogs containing L- and D-homoglutamine and L- and D-pyrohomoglutamic acid at positions 5 and 6
AUTHOR(S): Hashimoto, Tadashi; Uchida, Yoshiki; Nishijima, Miwako; Sakura, Naoki; Hirose, Kyoko
CORPORATE SOURCE: Sch. Pharm., Hokuriku Univ., Kanazawa, 920-11, Japan
SOURCE: Bull. Chem. Soc. Jpn. (1987), 60(3), 1207-9
CODEN: BCSJA8; ISSN: 0009-2673
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Six title substance P (SP) analogs were prepd. by the solid-phase method on a benzylhydrylamine resin. The smooth muscle contractile activities of these analogs were compared with the activity of SP on isolated guinea pig

ileum and trachea. The potency of [D-Hgn5,Hgn6]-SP (Hgn = homoglutamine residue) was as high as that of SP in the guinea pig ileum assay. The replacements of both Gln residues at positions 5 and 6 with the Hgn-D-Hgn sequence brought a drastic decrease in activity. The D-pyroHgu-Hgn-Phe-Phe-Gly-Leu-Met-NH2 (pyroHgu = pyrohomoglutamic acid) analog possessed the highest potency among the 6 analogs.

IT **111139-27-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and smooth muscle-contracting activity of)

L29 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:515964 CAPLUS
DOCUMENT NUMBER: 107:115964
TITLE: Synthesis and biological activities of D-homoglutamine analogs of substance P
AUTHOR(S): Hashimoto, Tadashi; Uchida, Yoshiki; Nishijima, Miwako; Moro, Tadashi; Sakura, Naoki; Hirose, Kyoko
CORPORATE SOURCE: Sch. Pharm., Hokuriku Univ., Kanazawa, 920-11, Japan
SOURCE: Bull. Chem. Soc. Jpn. (1986), 59(12), 4009-11
CODEN: BCSJA8; ISSN: 0009-2673
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Substance P (SP) analogs H-Arg-Pro-Lys-Pro-X-X1-Phe-Phe-Gly-Leu-Met-NH2 [X-X1 = D-Hgn-Gln (Hgn = homoglutamine), Gln-O-Hgn, D-Hgn-D-Hgn] and H-Pro-X-X1-Phe-Phe-Gly-Leu-Met-NH2 (I, X-X1 = same) were prepd. by the solid-phase method on a benzhydrylamine resin using a Beckman System 990C Peptide Synthesizer. The biol. activities of the peptides were assayed on the smooth muscles of isolated guinea pig ileum and trachea. The substitution of D-Hgn for Gln reduces the activity. I (X-X1 = Gln-O-Hgn) acted as a SP antagonist.

IT **110072-69-0P 110072-70-3P 110072-71-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and smooth muscle-contracting activity of)

L29 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:419101 CAPLUS
DOCUMENT NUMBER: 105:19101
TITLE: Biological profile of six putative substance P antagonists
AUTHOR(S): Growcott, J. W.; Briggs, I.; Jamieson, A.; Dutta, A. S.; Gormley, J. J.
CORPORATE SOURCE: ICI Pharm. Div., Macclesfield/Cheshire, SK10 4TG, UK
SOURCE: Fernstroem Found. Ser. (1985), 6(Tachykinin Antagonists), 345-54
CODEN: FFOSDF; ISSN: 0167-7004
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Six putative substance P antagonists were studied in a no. of different prepns. to det. their activities as inhibitors of substance P [33507-63-0] and substance P(6-11) [51165-07-2], as analgesics, as inflammation inhibitors, and in stimulating histamine [51-45-6] release. Behavioral and muscular control side effects were also measured. Most of the compds. preferentially antagonized substance P(6-11), presumably reflecting a receptor subtype selectivity of these compds. No conclusive antinociceptive activity could be demonstrated that was not assocd. with interfering side effects.

IT **102966-11-0**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(biol. activity of, specificity of)

L29 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:418675 CAPLUS

DOCUMENT NUMBER: 105:18675
TITLE: Antagonists of substance P. Further modifications of SP antagonists obtained by replacing either positions 7, 9 or 7, 8 and 11 of SP with D-amino acid residues
AUTHOR(S): Dutta, Anand S.; Gormley, James J.; Graham, Anthony S.; Briggs, Ian; Growcott, James W.; Jamieson, Alec
CORPORATE SOURCE: Pharm. Div., Imp. Chem. Ind. PLC, Macclesfield/Cheshire, SK10 4TG, UK
SOURCE: J. Med. Chem. (1986), 29(7), 1171-8
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Antagonists of substance P (SP) [33507-63-0] and the C-terminal (6-11)-hexapeptide [51165-07-2] were obtained by multiple D-amino acid substitutions in various positions of SP and by protecting the N.alpha.-arginine-1 and N.epsilon.-lysine-3 amino groups with benzyloxycarbonyl groups. On the guinea pig ileum a no. of these antagonized both SP and the hexapeptide. Except for [N.alpha.-Z-Arg1,D-Pro2,N.epsilon.-Z-Lys3,Asn5,Arg6,D-Phe7,D-Trp9]-SP-OMe [101835-64-7] and the corresponding amide, which were more potent antagonists of SP than the hexapeptide, all the others, e.g., [N.alpha.-Z-Arg1,D-Pro2,4,N.epsilon.-Z-Lyz3,D-Phe7,8,Sar9,D-Met11]-SP-OMe [101835-69-2] and [N.alpha.-Z-Arg1,D-Pro2,4,N.epsilon.-Z-Lys3,D-Phe7,8,Sar9,MeLeu10,D-Met11]-SP-OMe [101835-71-6] were more potent antagonists of the hexapeptide. On the rat spinal cord prepn., most of the antagonists were only active against the hexapeptide. A few antagonized SP, but these also reduced carbachol [51-83-2] or both carbachol and glutamate [56-86-0] responses. Two of the antagonists, [D-Pro2,Asn5,Lys6,D-Phe7,D-Trp9]-SP-OMe [101835-62-5] and [Boc-D-Pro4,D-Phe7,8,Sar9,D-Met11]-SP(4-11)-OMe [101835-70-5], were inactive on the ileum but still antagonized the hexapeptide on the spinal cord. The smallest peptides to antagonize SP and the hexapeptide were 2 heptapeptides, with [Z-Asn5,Arg6,D-Phe7,8,Gly9(CH2S)D-Leu10,D-Met11]-SP(5-11)-OMe [101835-77-2] being more potent than [Boc-Asn5,Arg6,D-Phe7,D-Trp9]-SP(5-11)-OMe [101835-66-9]. None of the antagonists showed significant analgesic activity without side effects. Some of the antagonists released histamine [51-45-6] from isolated rat peritoneal cells.

IT **101915-11-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and deprotection and substance P antagonist activity of)

IT **101835-73-8P 101835-74-9P 101835-76-1P**
101915-12-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and substance P antagonist activity of)

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